In The

Supreme Court of the United States

October Term, 1973

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No. 73-168

MARKO DUROVIC, an individual and also known as MARKO DUROVIC, formally d/b/a DUGA LABORATORIES; STEVAN DUROVIC, d/b/a PROMAK LABORATORIES; and KREBIOZEN RESEARCH FOUNDATION, a corporation,

Petitioners,

vs.

CASPAR W. WEINBERGER, Secretary of Health, Education & Welfare, and ALEXANDER M. SCHMIDT, Acting Commissioner of Food & Drugs,

Respondents.

PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SEVENTH CIRCUIT

SOLOMON H. FRIEND
JEROLD W. DORFMAN
Attorneys for Petitioners
16 West 61st Street
New York, New York 10023
(212) 245-7052

DAVID A. BEALE
Legal Assistant on the Petition

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TO: THE HONORABLE, THE CHIEF JUSTICE AND ASSOCIATE JUSTICES OF THE SUPREME COURT OF THE UNITED STATES

The petitioners pray that a writ of Certiorari issue to review the judgment of the United States Court of Appeals for the Seventh Circuit granting summary judgment for the respondents.

Opinions of the Courts Below

The opinion of the United States Court of Appeals for the Seventh Circuit in Marko Durovic, et. al. v. Elliot Richardson, Secretary of Health, Education & Welfare, et. al., No. 71-1658 was entered on April 25, 1973, but is not yet officially reported. It is printed in the Appendix to this Petition.

The order of the United States District Court for the Northern District of Illinois, No. 69 C32, was entered on May 18, 1971, and is also appended hereto.

Jurisdiction

The judgment and opinion of the Court of Appeals were entered on April 25, 1973. The jurisdiction of this Court is invoked under 28 U.S.C. §1254(1).

Questions Presented for Review

1. Have plaintiffs been unfairly denied an opportunity to present persuasive evidence, in contravention of the Due Process Clause of the Fifth Amendment, to show the general recognition of safety of their drug, Krebiozen, within the meaning of Section 21 U.S.C. §321(p), prior to the 1962 Amendments to the Federal Food, Drug and Cosmetic Act of 1938?

2. Did the requirement of "safety" in the Federal Food, Drug and Cosmetic Act of 1938, prior to the 1962 Amendments, include the concept of efficacy, or was "safety" synonymous with "non-toxicity?"

Questions Presented for Review

3. Is the issue of knowledge of Krebiozen's identity and composition prior to the 1962 amendments a question of fact to be decided at a trial on the merits?

4. Are petitioners entitled to a hearing on the question of efficacy of Krebiozen, if that concept is deemed included in the requirement of general recognition of "safety," as "safety" was understood to be prior to the 1962 Amendment?

5. Is petitioners' drug "grandfathered" under §107(c)(4), 76 Stat. 789, of the 1962 Amendments to the Federal Food, Drug & Cosmetic Act of 1938, 52 Stat. 1040?

6. Are petitioners entitled to a hearing on the question of the qualification of the government's experts upon whose opinions the non-recognition of the safety of Krebiozen was grounded by the District Court and Court of Appeals, where under the applicable statute (21 U.S.C. §321(p), such recognition (or non-recognition) must be by "experts qualified by scientific training and experience to evaluate the safety of drugs?"

Constitutional and Statutory Provisions Involved

The Constitution provision involved is the Fifth Amendment to the United States Constitution. The statutory provisions involved are the Federal Food, Drug & Cosmetic Act of 1938, 21 U.S.C. §301 et seq., prior to the Drug Amendment Act of 1962, 76 Stat. 789, and the Act, as amended, and also the Administrative Procedure Act, 5 U.S.C. §§701-704. All pertinent provisions of the above are set forth in the Appendix.

Statement of Facts

Plaintiff Marko Durovic is a resident of the City of Chicago and is the owner of Duga Laboratories, the successor to Duga Biological Institute. He is also possessed of a power of attorney for Plaintiff Dr. Steven Durovic the sole owner of Plaintiff Promak Laboratories, located in Chicago, Illinois. Plaintiff Krebiozen Research Foundation is an Illinois corporation, its place of business located in Chicago. The defendants are the Secretary of the Department of Health, Education and Welfare and the Acting Commissioner of the Food and Drug Administration, an agency of the Department of Health, Education and Welfare.

From 1951 and at all times thereafter material, plaintiffs have manufactured and/or distributed in interstate commerce a drug product called Krebiozen as an agent for use in the management and treatment of malignant tumors.

In 1964 an indictment was filed by the United States of America in the United States District Court, Northern District of Illinois, against the plaintiffs (64 CR 668) alleging in numerous counts inter alia, that Krebiozen was a new drug as defined by Section 201(p) of the Act (21 U.S.C. 321(p)) and had been introduced and delivered for introduction into interstate commerce from on or about April 15, 1954 to on or about October 19, 1964, contrary to the provisions of Section 505 of the Act, in that approval of a New Drug Application, filed pursuant to Section 505(b), was not effective with respect to such drug and the drug was not exempt as an investigational drug since the drug had been distributed in interstate commerce for

commercial purposes. The said indictment came on for a jury trial and after nine months of trial, a verdict of acquittal in favor of all of the plaintiffs herein was returned by the jury, and judgments of acquittal entered on the verdict.

On May 3, 1968 defendants served upon plaintiffs a "Notice of Hearing" pursuant to Section 305 of the Federal Food, Drug and Cosmetic Act (the Act), (21 U.S.C. §335), informing plaintiffs that investigation by the Food and Drug Administration (FDA) indicated plaintiffs' responsibility for criminal violations of the Act in that plaintiffs had delivered and caused to be delivered to various persons in 1967 and 1968 for introduction into interstate commerce quantities of Krebiozen in violation of the New Drug Provisions of Section 505 of the Act, in that no New Drug Application filed pursuant to Section 505(b) was effective with respect to said drug and that it was not exempt as provided for by the "Grandfather" provision of the said Act, (Section 107(c)(4) of the 1962 Amendment to the Act, 76 Statute 789). The said Notice of Hearing further informed plaintiffs that an informal hearing on the charges would be held on June 11, 1968 and that if no response was received on or before the date set, a decision would be made as to whether to refer the matter to the Department of Justice for criminal prosecution. On June 6, 1968 plaintiffs informed the FDA that they had not engaged in the acts claimed to be violative of the Act and urged that no criminal action should be taken against the plaintiffs.

Statement of Facts

Plaintiffs on January 7, 1969, filed their complaint for a declaratory judgment, under 28 U.S.C. §§1337 and 2201, setting forth two causes of action, claiming that plaintiff's drug product, known as Krebiozen, was exempt from the aforesaid new drug provisions of the Act, by reason of the "Grandfather Provisions" of the Drug Amendments Act of 1962.

The petitioners allege an exemption on the ground that on the day preceding the enactment date of the 1962 Amendments, Krebiozen was, (a) commercially used or sold in the United States, and, (b) was not a "new drug" as defined in Section 201(p) of the basic Act as then in force, and, (c) was not covered by an effective NDA under Section 505 of the Act then in force.

The second cause of action alleges, in the alternative, that Krebiozen is exempt from the new drug provision of the Act, because on the day preceding the enactment date, an NDA, having been filed pursuant to Section 505(b) of the Act then in force, was in fact "effective" with respect to Krebiozen.

On March 17, 1969, the defendants filed their answer denying that Krebiozen was not a new drug prior to the enactment date of the 1962 Amendments; denying that Krebiozen was commercially used or sold prior to such date; denying that an effective NDA covered Krebiozen prior to the enactment date; and denying that there was an actual controversy, justicable in nature, between the parties, so as to give rise to the District

Court's exercise of discretion under 28 U.S.C. §2201.

Extensive pre-trial interrogatories by both sides resulted in the production and introduction into the record of numerous documents bearing upon the safety and effectiveness of Krebiozen, and the general recognition thereof by qualified experts.

The government's main line of defense was that the drug, Krebiozen, was not exempt from the 1962 Amendments, because it was never generally recognized by qualified experts as "safe", prior to the enactment date, and therefore, was a "new drug" on that date and not entitled to the exemption provided in the 1962 Amendments. The Government's position was further based upon the supposition that the definition of "safety" was, in a drug used for a life threatening disease, the same as, and synonymous with "effectiveness". That is, a drug not generally recognized as "effective" for the treatment of a life threatening disease, could not have been generally recognized as "safe", and this, the Government contends was the law prior to the 1962 Amendments which, by statute, introduced the concept of "effectiveness", for the first time, in defining "new drug" under the Act.

Plaintiffs opposed this position contending that Krebiozen had been generally recognized as "safe" since 1954, and therefore was not a "new drug" on the enactment date of the 1962 Amendments; and therefore qualified for the exemption from

Section 505 under the said Amendments. Plaintiff, furthermore, introduced evidence to show that "safety" under the Act, prior to the enactment date, was generally understood, and enforced, to mean "non-toxic", without any requirement of effectiveness, whether or not the drug in question was used in life threatening diseases. In any event, plaintiff also introduced evidence to show that Krebiozen is effective, and was generally recognized as such, by qualified experts.

On December 12, 1970, Judge Perry granted leave to both sides to file simultaneous motions for summary judgment, and, after reviewing the parties' briefs, and evidence in the record, entered judgment, and an order, dated May 18, 1971, granting defendants' motion, denying plaintiff's motion and dismissing the plaintiff's complaint (See Appendix to Petition.).

On June 10, 1971, plaintiffs filed their Notice of Appeal.

On June 21, 1971, certain individuals who were not parties to this proceeding, petitioned the District Court for leave to intervene as plaintiffs, requesting the supersedeas bond be set and the effective date of Judge Perry's order stayed. The parties claimed to be cancer patients dependent upon Krebiozen for the control of their disease, whose very lives were endangered by Judge Perry's order.

Judge Perry denied their motion on the ground he lacked jurisdiction to allow intervention after Notice of Appeal. However, he allowed their

counsel, with the consent, and on behalf of plaintiffs, to file for supersedeas bond, and a stay of judgment, which motions were granted.

On June 24, 1971, defendants appealed, contending that the order, staying Judge Perry's judgment specifically providing that those who were receiving Krebiozen from the date of the filing of plaintiff's complaint, could continue to receive the drug, was improper. On July 2, 1971, the Seventh Circuit Court of Appeals by the Hon. Judge Wilbur Pell, Jr., reversed Judge Perry's decision and dissolved the stay of judgment, finding "no persuasive reason...in this posture of the litigation..." to allow a limited group of "customers" to receive Krebiozen with court approval "notwithstanding the entry of a judgment" dismissing plaintiff's complaint.

On July 14, 1971, plaintiffs filed a motion in the District Court, pursuant to Rule 60(b)(6) of the Federal Rules of Civil Procedure, requesting that Judge Perry reconsider the dismissal of plaintiff's complaint, in the light of two recent District Court decisions, which had not been published at the time the parties submitted their briefs on summary judgment. The two cases, were U.S.V. Pharmaceutical Corporation v. Richardson, (CCH Federal Food, Drug and Cosmetic Reporter—Paragraph 40483; published June 9, 1971, E.D., Va., decided April 1, 1971, (rev'd) 461 F.2d 223 (4th Cir. 1972), aff'd. U.S. ___, 41 U.S.L.W. 4861 (1973)), and U.S. v. An Article of Drug...Excedrin P.M. (CCH Federal Food, Drug and Cosmetic Reporter—Paragraph 40486; pub-

lished June 13, 1971, E.D., N.Y.; decided March 5, 1971, not officially reported).

Plaintiffs contended that the U.S.V. case was relevant in showing the District Court, in its order of May 18, applied the wrong statutory standard of "new drug" to the plaintiff's product.[1] The Excedrin P.M. case, furthermore, held, that merely because a dispute existed between the affidavits of "experts" on the question of general recognition of safety or effectiveness, this was no cause for the granting of summary judgment to the Government, which had argued that such a dispute in the affidavits, demonstrated, ipso facto, the lack of general recognition.

Judge Perry denied plaintiff's motion for reconsideration stating:

> "The court finds that said motion is not without merit, but considers that since it would only dispose of part of the litigation, that it would be more appropriate for the United States Court of Appeals to consider an expedited appeal and decide all other litigation in one final order." (Emphasis ours.)

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1. Paragraph 6 of Judge Perry's Findings of Fact States: "The affidavits of Dr. Steinfeld and Dr. Baker establish that there is no general recognition among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that Krebiozen is now or has ever been safe or effective for the management or treatment of malignant tumors." (Emphasis ours).

Statement of Facts

On June 20, 1972, an appeal was argued in the United States Court of Appeals for the Seventh Circuit, before Fairchild, Cummings and Stevens, Circuit Judges. On April 25, 1973, a judgment was handed down affirming the order of the District Court.

The Seventh Circuit first decided that the two New Drug Applications (NDA's) filed by petitioners in 1954 and 1961 were incomplete and thus not adequately filed.

The Seventh Circuit then decided petitioners' "Grandfather" claim under §107(c)(4), 76 Stat. 789, of the Drug Amendments of 1962. The court found for petitioners on Grandfather Requirement (A), that Krebiozen was "commercially used or sold" prior to October 9, 1962.

The present controversy concerns Grandfather Requirement (B), whether Krebiozen was "generally recognized as safe" as that concept was understood to be as of October 9, 1962. In spite of the strong, affirmative affidavits in support of Krebiozen, the Seventh Circuit held the drug was not generally recognized as safe. In so holding, but without so referring, the court necessarily decided there was no triable issue of fact as to Krebiozen's safety, regardless of its long history and without giving petitioners the opportunity for presenting evidence.

The Seventh Circuit based its decision on two alternate theories. First, it held that the concept of safety in the law before the 1962 Amendments included the concept of efficacy for the indicated use of the drug where it is used in the treatment of life-threatening disease. Petitioners emphatically disagree with this conclusion, as it was not the intent of Congress prior to 1962, and certainly was not the understood definition of safety in the field of drug law prior to 1962.

The second and alternate theory of the Seventh Circuit was that since Krebiozen's identity and composition were "unknown," the drug could not possibly be recognized as safe. Petitioners, of course, had offered probative evidence to contradict both "findings," and submit that such questions are one of fact and should be decided after trial.

Grandfather Requirement (C) was not in issue, as the government contended that Krebiozen has never been covered by an effective NDA.

Reasons for Granting the Writ

I.

THE COURTS BELOW, IN GRANTING DEFENDANTS' MOTION FOR SUMMARY JUDGMENT, HAVE DENIED PLAINTIFFS THEIR RIGHT TO BE HEARD AND TO PRESENT PERSUASIVE EVIDENCE DESPITE THE PRESENCE OF GENUINE AND MATERIAL QUESTIONS OF FACT.

Reasons for Granting the Writ

In an appeal from summary judgment an appellate court must resolve all disputed questions of fact in favor of the Appellant, Goodis v. United Artists Television, Inc., 425, F.2d 397, 405 (2d Cir. 1970), and such a plaintiff must be given the benefit of every doubt. Bryan v. Aetna Casualty and Surety Company, 381 F.2d 872 (8th Cir. 1967).

The Seventh Circuit erred in not giving plaintiffs these presumptions and thus denied plaintiffs of their day in court. Plaintiffs only pray for an opportunity to present their evidence before an impartial fact finder concerning the general recognition safety of their drug, as "safety" was understood prior to the enactment date of the 1962 Amendments to the Act.

Indeed, the Seventh Circuit even noted that there was a genuine controversy surrounding plaintiffs' drug, but refused to consider it in disposing of the case!

> "We have been made aware, in this record, of much of the emotionally charged controversy about Krebiozen. Some characterize Krebiozen as a hoax, yet there are many who believe with deep sincerity that a number of cancer sufferers have been aided, or even saved, by it. Its advocates contend that the medical "establishment" both in and out of government has unfairly denied Krebiozen a reasonable test. So distinguished a person as the Honorable Paul Douglas, former Senator from Illin-

ois, has taken its part. Some would argue that if a substance is found to be innocuous, a sufferer who hopes it will relieve him is entitled to have it.

The issues suggested by the last paragraph, however, are not before us for decision." (App. 13, supra.)

There are documents which will show that the FDA and the "medical establishment" are biased against Krebiozen.[2] This bias has so far

2. One document, a HEW News Release of September 7, 1963 entitled "Results of Analysis of 'Krebiozen' ", identified petitioners' drug as creatine. Krebiozen is not and never has been creatine. The news release, reprinted in the Appendix, was deliberately released just prior to the time the National Cancer Institute Committee reviewing Krebiozen was to make its report. Once the Committee was aware of the news release, there was no way it could issue a favorable verdict without "losing face" before the medical establishment. Indeed, the Institute Committee subsequently declined to undertake clinical testing of Krebiozen. See HEW Release of October 16, 1963.

Three other documents, HEW Releases of January 30, 1966, January 31, 1966, and March 31, 1966, also reprinted in the Appendix, dramatically show the great prejudice the FDA has against Krebiozen. Despite having lost the criminal proceedings against petitioners, the FDA vowed to do "whatever will be necessary to keep Krebiozen out of interstate commerce." (Release of January 31, 1966). Surely, petitioners cannot hope to obtain an impartial hearing before such an agency!

See also the Affidavit of petitioner Marco Durovic (77a) in which he portrays the history of Krebiozen. This Affidavit depicts with detail some of the specific acts of prejudice by the medical "establisnment," and also shows the great frustration petitioners have faced in order to have their work recognized.

(Cont'd)

prevented petitioners from obtaining a fair and reasonable trial on the safety of their drug, in which they may present evidence before an impartial fact finder. It is to this main point petitioners hopefully seek redress.

Such foreclosure to plaintiffs of a fair and reasonable hearing on a genuine and substantial question of fact is tantamount to a denial of the Constitutional guarantees of due process under the Fifth Amendment. This Court has long been careful to protect such constitutional rights. In 1913 in Saunders v. Shaw, 244 U.S. 317, petitioner had brought a writ of error claiming deprivation of due process of law contrary to the Fourteenth Amendment because the case had been decided against him without his ever having had the proper opportunity to present evidence. Though it appeared that the Court was remanding for a mere technicality, and that the facts were against the petitioner, Mr. Justice Holmes, speaking for the Court, asserted:

> "...but we do not see in the record an absolute warrant for the assumption and therefore cannot be sure that the [petitioner's] rights are protected without giving him a chance to put his evidence in" (244 U.S. at 319).

(Cont'd)
Also appended is a copy of the Proposed Joint Resolution of the 88th Congress (S.J. Res. 101 of July 18, 1963) in which $250,000 was to be authorized for a fair and impartial test of Krebiozen by the National Institute of Health (97a). The bill did not pass and such a test for efficacy as mentioned above, was never undertaken by the government.

Reasons for Granting the Writ

More recently, this Court has affirmed these constitutional concepts in its decision in Fuentes v. Shevin, 407 U.S. 67, 92 S.Ct. 1983 (1972). There the Court upheld the "constitutional right to be heard" before a deprivation of property. Mr. Justice Stewart, speaking for the Court, asserted that:

> "The constitutional right to be heard is a basic aspect of the duty of government to follow a fair process of decision-making when it acts to deprive a person of his possessions. The purpose of this requirement is not only to ensure abstract fair play to the individual. Its purpose, more particularly, is to protect his use and possession of property from arbitrary encroachment--to minimize substantively unfair or mistaken deprivations of property, a danger that is especially great when the State seizes goods... The prohibition against the deprivation of property without due process of law reflects the high value, embedded in our constitutional and political history, that we place on a persons' right to enjoy what is his, free of governmental interference.... The requirement...to be heard raises no impenetrable barrier... But the fair processs of decision-making that it guarantees works, by itself, to protect against arbitrary deprivation of property. For when a person has an opportunity to speak up in his own defense, and when the State must listen to what he has to say, substantially unfair and mistaken depriva-

tions of property interests can be prevented" 407 U.S. at 80-81, 92 S. Ct. at 1944.

Mr. Justice Powell in his concurring opinion in Weinberger v. Hynson, Westcott and Dunning, Inc. ___U.S.____, ____S.Ct.____, 41 U.S.L.W. 4848 (1973) recognized these serious constitutional issues that are present in the drug field. In that case, however, Mr. Justice Powell was referring to denial of a hearing for efficacy. Petitioners are here concerned with denial of a hearing for safety, since Krebiozen is asserted to be "grandfathered" and thus exempt from the efficacy requirement. Mr. Justice Powell also noted that due process questions had not been squarely presented in that case, and thus were not ripe for judicial consideration. Petitioners herein submit that such due process issues (i.e. refusal of hearing with summary judgment) are squarely presented and ripe for judicial review in the case at bar, and pray that the Court so grant their writ of certiorari.

As the record of this case will show, there is much dispute and controversy over petitioners' investigations and supporting affidavits. Denial of a hearing on these material and substantial issues of fact will result in a final and complete deprivation of petitioners' constitutional safeguards of due process.

Petitioners further submit that they are not only interested in their own deprivation of property without due process of law, but are deeply concerned with the untold thousands of suffering can-

cer patients who could be helped with Krebiozen. Mr. Justice Powell, in footnote 2 of his concurring opinion expressed his own concern when he noted that "[i]n an understandable zeal to remove the [drugs], an administrative agency must not overlook both the interest of the public and the right of the proprietor in protecting the drugs that are useful in the prevention, control or treatment of illness" ___U.S. at___, ___S.Ct. at____, 41 U.S.L.W. at 4857, fn. 3 (1973).

II.

THE QUESTIONS OF LAW PRESENTED HERE WERE NOT AT ISSUE IN THE RECENTLY DECIDED "NEW DRUG" CASES.

Petitioners' drug Krebiozen, was never the subject of an effective New Drug Application under the Federal Food, Drug and Cosmetic Act of 1938, 52 Stat. 1040, and is therefore distinguishable from the following cases recently decided by this Court.

Weinberger v. Hynson, Westcott and Dunning, Inc., ___U.S.___, ____S.Ct.____, 41 U.S.L.W. 4848 (1973), dealt with Lutrexin, a drug that was deemed safe under the 1938 Act, when a new Drug Application was granted, but was appraised ineffective by a panel of NASNRC. Part I of the opinion covered prewithdrawal hearings, while Part II discussed the efficacy requirement under Section 201(p).

Reasons for Granting the Writ

Petitioners' drug is exempt from the requirement of efficacy because it is alleged by petitioners to be "grandfathered." That is, prior to the 1962 Amendments, it was "commercially used or sold in the United States," was not a new drug under the 1938 Act (because it was generally recognized as safe), and was not covered by an effective new drug application. (§107 (c)(4) of 1962 Amendments, 76 Stat. 789.)

The controversy over Krebiozen is over the second grandfather requirement of safety and it is to this issue petitioners respectfully request an impartial hearing on the facts.

Ciba Corp. v. Weinberger, ___U.S.___, ___S.Ct. ___, 41 U.S.L.W. 4857 (1973), also dealt with questions of withdrawal of a New Drug Application in deciding that the FDA has jurisdiction in an administrative proceeding to determine whether a drug product is a "new drug".

Krebiozen has not reached the stage of ritonic capsules, the drug in that case, because Krebiozen is alleged by petitioners to be "grandfathered". Nevertheless, petitioners in addition to their rights under the declaratory judgment statute, are entitled to judicial review of the FDA "ruling", under the Administrative Procedure Act, 5 U.S.C. §§701-704, that their drug is a "New Drug," especially if there is an abuse of discretion, or bias. Overseas Media Corp. v. McNamara, 385 F.2d 308, 316 (D.C. Cir. 1967), Treat v. SEC, 306 F.2d 260 (C.A.D.C. 1962).

Reasons for Granting the Writ

In the Bentex case, ___U.S.____, ___S.Ct. ___, 41 U.S.L.W. 4858 (1973), the Court held that the FDA had initial jurisdiction to decide "new drug" and "grandfather" issues. Petitioners submit that since the FDA is biased against Krebiozen, and has initially denied both its request for "grandfather" status and "effective" New Drug Application status, petitioners are entitled to a hearing before an impartial fact finder, Fuentes v. Shevin, supra. Petitioners are ready to present to such a fact finder "substantial evidence" which will characterize an adequate and well-controlled clinical investigation" Hynson, supra.

The U.S.V. Pharmaceutical Corp. v. Weinberger decision, ___ U.S. ___, ___S.Ct. ___, 41 U.S.L.W. 4861 (1973), is not dispositive of the petitioners' issues either. The drugs in question there were two "Me-too" drugs which had never been covered by effective NDA's, and seven related drugs which had been covered, but with their applications later withdrawn.

The "me-too" drugs at first glance might be deemed to encompass the same issues as Krebiozen since they were all drugs which had never been covered by effective NDA's. However, there is a sharp distinction to be made between "me-too" drugs and Krebiozen. Krebiozen is an individual product, discovered and owned by individuals, and no related or similar product has been subject to an "effective" New Drug Application, or a withdrawal of approval of such application by the FDA.

As the Court noted in U.S.V., supra, if any of the generic drugs are covered by an "effective" NDA, none of them are exempt from the efficacy requirements of §201(p). USV at 4864.

It is submitted by petitioners, therefore, that the issues presented here, in this petition for a writ of certiorari, have not been before this Court for review, and are of great importance not only to petitioners and their cancer patients, but also to other drug manufacturers of drugs that were generally recognized as safe before 1962, or were otherwise never covered by an "effective" New Drug Application.

III.

THE COURT OF APPEALS FOR THE SEVENTH CIRCUIT ERRED IN TWO RESPECTS.

a. The concept of safety in the law before the 1962 Amendments did not include the concept of effectiveness.

If an administrative agency were able to unilaterally and ex post facto add the requirement of efficacy to the law before the 1962 Amendments, it would be a violation of the Constitution. It is a well established concept of our constitutional scheme that the function of executive and administrative bodies is to enforce and administer the laws as written by Congress and as interpretated by the Courts. Although the executive and administrative officers may exercise some discretion, they may not exceed legislative author-

ity. See H.K. Porter Co. v. N.L.R.B., 397 U.S. 99 (1970); United States v. United States District Court for Eastern District of Michigan, 444 F.2d 651 (6th Cir. 1971), aff'd. 407 U.S. 297 (1972).

The Seventh Circuit erred in holding that the concept of safety included the concept of efficacy. Such a holding would seem to be contra to Congressional intent before 1962. It is apparent that in passing the 1962 Amendments, Congress expressly decided to add the requirement of efficacy, but in so doing also included a "grandfather" clause to exempt drugs that had met the previously singular requirement of safety. If Congress had meant to include efficacy before 1962, there would be no need for such a "grandfather" clause. The Seventh Circuit by its determination below held that the "grandfather" clause was without effect, resulting in a decision that is opposite to Congressional intent.

b. The issues of Krebiozen's identity and composition, as well as the ultimate issue of safety are questions of fact that should be decided at a trial on the merits.

The Seventh Circuit erred when it held as a matter of law that Krebiozen could not be recognized as safe because it was allegedly unknown. Such issues are questions of fact for the trier of facts. Petitioners stand ready with "substantial evidence" to show not only that Krebiozen's identity and composition were sufficiently known, but also that it was completely "safe", as that term was understood under the 1938 Act, and generally recognized as such.

In any event, as heretofore stated, in an appeal from summary judgment, appellants are entitled to the benefit of every doubt. Goodis, supra; Bryan, supra. The Seventh Circuit did not give this additional weight to the evidence before it.

IV.

IF THE CONCEPT OF SAFETY IN THE LAW BEFORE THE 1962 AMENDMENTS DID INCLUDE THE CONCEPT OF EFFICACY, THEN PETITIONERS SHOULD BE GIVEN A HEARING ON THIS QUESTION.

The issue of efficacy is a factual one and petitioners are entitled to a chance to present evidence at an impartial hearing. Fuentes, supra. Petitioners submit that they have more than enough "substantial evidence", as defined in §505 (d) of the Act, to pass over the "threshold". This evidence is typified by a study made by Dr. A.C. Ivy in 1951 in which he found Krebiozen both safe and effective. See Affidavit of Dr. Ivy appended to this petition.

Petitioners, therefore, pray that if this Court deems that drugs such as Krebiozen had to be effective as well as safe prior to 1962 in order to qualify for "grandfather" status, then petitioners respectfully request the Court to remand for an evidentiary hearing so that they may have their day in court.

Conclusion

Petitioners ask for relief from this Court of last resort not only for themselves, but for countless suffering cancer patients who possibly may be aided by Krebiozen, and who have thus far been denied the satisfaction of having the status of Krebiozen squarely and fully litigated.

WHEREFORE, for the above and foregoing reasons, it is respectfully submitted that the Writ of Certiorari requested hereby should be issued and the opinion and judgment of the Seventh Circuit Court of Appeals reversed.

Respectfully submitted,

SOLOMON H. FRIEND
JEROLD W. DORFMAN
Attorneys for Petitioners

DAVID A. BEALE
Legal Assistant on the Petition

Dated: July 20, 1973

Opinion of the United States Court of Appeals for the Seventh Circuit

IN THE

UNITED STATES COURT OF APPEALS

FOR THE SEVENTH CIRCUIT

September Term, 1971 April Session, 1972

No. 71-1658
MARKO DUROVIC, an individual and also known as MARKO DUROVIC, formerly d/b/a DUGA LABORATORIES: STEVAN DUROVIC, d/b/a PROMAK LABORATORIES and KREBIOZEN RESEARCH FOUNDATION, a corporation,

Plaintiffs-Appellants,

v.

ELLIOT RICHARDSON, Secretary of Health, Education & Welfare, and CHARLES C. EDWARDS, Commissioner of Food & Drugs,

Defendants-Appellees.

ARGUED JUNE 20, 1972 - DECIDED APRIL 25, 1973

Appeal from the United States District Court for the Northern District of Illinois, Eastern Division, 69 C 32

J. SAM PERRY, Judge.

Opinion

Before Fairchild, Cummings, and Stevens, Circuit Judges.

FAIRCHILD, Circuit Judge. Plaintiffs appeal from an unfavorable declaratory judgment entered on defendants' motion for summary judgment in plaintiffs' action for declaratory relief.

Plaintiffs are interested in the manufacture and distribution of the "drug product called Krebiozen as an agent for use in the management of malignant tumors." Defendants are charged with administration of the Federal Food, Drug and Cosmetic Act, as amended. 21 U.S.C. Section 355(a) prohibits the introduction of a "new drug" into interstate commerce unless an approval of a new drug application under Section 355(b) (an NDA) is effective.

21 U.S.C. Section 335 calls for notice to a proposed defendant before a violation is reported to a United States attorney. Such notice was given to plaintiffs. Although Section 335 also calls for an opportunity [1] administratively, for presentation of views, it does not contemplate a proceeding leading to a final administrative order, subject to statutory judicial review. As a result of the notice, and, apparently, defendants' rejection of views that sale of Krebiozen in interstate commerce required no effective NDA, plaintiffs brought this action. They sought a declaration (1) that Krebiozen is not a new drug by reason of the operation of a "grandfather" provision, enacted in

1. Such opportunity is not a prerequisite to prosecution. United States v. Dotterweich, 320 U.S. 277, 279 (1943) rehearing den. 320 U.S. 815.

1962, in other words, that Krebiozen was commercially sold or used and not a "new drug" under the law just before the 1962 amendments, or, alternatively (2) that if Krebiozen was a new drug, one or more NDA's became effective, one in 1954 and one in 1961.

Each side moved for summary judgment. The district court entered judgment that "Krebiozen is now and has always been a new drug within the meaning of the statutory definition for which no approved New Drug Application is now or has ever been effective." Findings and conclusions are reported at 327 F. Supp. 386. Plaintiffs appealed. We affirm.

Since summary judgment was granted, the questions on appeal are whether there was no genuine issue as to any material fact and whether the propositions declared were correct as a matter of law.

Plaintiffs' alternative claims, that of grandfather clause exemption because Krebiozen was not a new drug under the 1938 law, and that of an effective NDA under the 1938 law are inconsistent. Although plaintiffs chose to press the grandfather clause claim first, chronology makes it more logical to take up their claims in the opposite order.

I. The 1954 and 1961 NDA's.

Plaintiffs' activity in the United States with Krebiozen, previously unknown, began in 1949-1951. Undeniably it was then a new drug as defined in sec. 201(p) of the 1938 act. 52 Stat. 1040, then in force. Under sec. 505(a), unless an NDA was on file and effective, a new drug could not be introduced into

interstate commerce except under regulations covering solely investigational use.

On April 15, 1954, consistently with the new drug status of Krebiozen, plaintiff Marko Durovic tendered an NDA. On May 25, 1954, the Secretary replied by letter stating that the application was incomplete in two particulars and accordingly that it may not be filed.

Plaintiffs contend that this NDA became effective by operation of law, 60, or at most 180, days after receipt. They rely on sec. 505(b)and (c). If this NDA were deemed an application filed when received, within the meaning of (b), (c) would indeed cause it to become effective on the sixtieth day after the filing unless postponed by the Secretary to a time not more than 180 days after filing. Clearly there were no notice and hearing under (d) which would support an order refusing to permit the NDA to become effective, nor under (e) which would support an order suspending effectiveness.

Defendants' position is that a document purporting to be an NDA, received, but deemed incomplete, is not a filed application under (b), so as to become effective by lapse of time under (c).

Sec. 701(a) vested authority in the Secretary to promulgate regulations for the efficient enforcement of the act. In 1954, 21 C.F.R. Section 1.110 provided that an application shall not be accepted for filing if incomplete on its face by omission of required material, and called for notice to the applicant. We consider the regulation a reasonable means of determining the fact and time of filing an application and preventing the

triggering of the automatic operation of the statue where an intended application is incomplete under the statute. Notice of incompleteness, conforming to the regulation, was given. It does not appear either that Durovic amended the application so as to supply the omitted information, which would, under the regulation, have resulted in a filing date at the time of receipt of the amendment, if then complete, or that he challenged the refusal to accept for filing in any legal proceeding.

On March 27, 1961, Dr. Stevan Durovic, another plaintiff, submitted another NDA. This act was consistent with continued new drug status of Krebiozen. The application was supplemented March 31 and April 13. On May 23, 1961, the Director of the Division of New Drugs replied by letter stating that the application as amended was regarded as received April 13, that a preliminary review showed the NDA was incomplete in specified areas, but that there would be a further letter. On June 9, the Director wrote an eight page letter listing areas in which the NDA was incomplete and inadequate, and stating that, accordingly, it may not be filed.

The applicable regulation at this time was 21 C.F.R. 130.5. It was similar to the earlier one in all material respects, but also provided a procedure whereby the applicant, if he disputed the finding of incompleteness, could request filing over protest, and thus set the statutory machinery in motion. There is no claim that Dr. Durovic made such request.

Opinion

We consider the regulations valid and that the agency complied with them. Accordingly we conclude that neither the 1954 nor 1961 NDA was a filed application so as to cause it to become effective by operation of law with lapse of time.

II. The "grandfather" Claim.

Until 1962 the controlling definition of a new drug depended upon the lack of general recognition among experts that it was "safe" for use according to its labeling. The Drug Amendments of 1962 [2] enlarged the required general recognition to "safe and effective". 21 U.S.C. Section 321(p), as amended in 1962, reads in material part:

> "(p) The term 'new drug' means -
>
> (1) Any drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, . . . or
>
> (2) Any drug . . . the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used

2. P.L. 87-781, 76 Stat. 780.

> to a material extent or for a material time under such conditions." (We have underlined the words added by the Drug Amendments of 1938. All the other material quoted appeared in the 1938 act.)

The Drug Amendments of 1962 were approved October 10, 1962. Sec. 107(c)(4), 76 Stat. 789, a grandfather clause, provided:

> "In the case of any drug which, on the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section [321(p)] of the basic Act as then in force, and (C) was not covered by an effective [NDA] the amendments to section [321(p)] made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day."

The basic argument on behalf of plaintiffs is that on October 9, 1962, Krebiozen (A) was commercially used and sold in the United States, (B) was generally recognized as "safe" in the sense that it was non-toxic, and (C) was not, assuming their alternative argument be rejected, covered by an effective NDA. The basic argument of the government is (1) that, properly construed, the law before the 1962 amendments defined a drug which was to be used for treatment of a life-threatening disease as a new drug unless generally recognized as effective as well as otherwise safe; (2) that Krebiozen was not so recognized: (3) that its composition was not sufficiently known to enjoy

general recognition as "safe" even in the narrow sense; i.e., non-toxic; and (4) that since Krebiozen was sold only for investigational use, it was not commercially used or sold within the meaning of the grandfather clause.

Activities of plaintiffs have been inconsistent with their present claim that Krebiozen had become a "recognized" rather than a "new" drug by October 9, 1962. The presentation of an NDA in 1954 and in 1961 implied that Krebiozen was a new drug on those dates. In June, 1963, plaintiff Stevan Durovic submitted a "Notice of Claimed Investigation Exemption" (IND) which, although withdrawn after a month, carried the same implication. In April, 1966, plaintiff Marko Durovic, under power of attorney for Stevan Durovic, wrote a letter to the FDA, which he referred to in the text as an "investigational drug application" and a "Notice of Claimed Investigation Exemption." Although this purported claim for investigational exemption noted that it was without prejudice to the status achieved by the earlier NDA's, it was inconsistent with the present claim that Krebiozen had, by October 9, 1962, ceased to be a "new" drug. [3]

3. Krebiozen has been involved in a number of judicial proceedings. (a) Durovic v. Palmer, 342 F.2d 634 (7th Cir. 1965). Plaintiff Stevan Durovic unsuccessfully sought to challenge certain federal investigations in June, 1963 of the preparation of Krebiozen. The opinion reflects at least an assumption that Krebiozen was then a "new" drug, "being distributed ostensibly for investigational use. . . ." (b) Ivy v. Katzenbach, 351 F.2d 32 (7th Cir. 1965), cert. den. 382 U.S. 958. Ivy unsuccessfully sought to enjoin prosecution under an indictment and requested a court supervised clinical test of

(Cont'd)

Conceding that plaintiffs may not be irrevocably bound by their acts implying that Krebiozen had not become a "recognized" rather than "new" drug by October 9, 1962, nor by the assumptions in later judicial decisions that it was still a "new" drug, we proceed to analysis of the showings made on motion for summary judgment in the instant case.

Grandfather requirement (A): "commercially used or sold" October 9, 1962.

Defendants assert that all Krebiozen sold at or recently before the critical date was sold under a restrictive label, pursuant to 21 C.F.R. 130.3, i.e., "An Agent for Investigational use. If so labeled and sold only to a qualified Caution — New drug limited by Federal Law to investigational use." If so labeled and sold only to a qualified expert who promised to investigate the safety of the drug, the shipment was exempt from 21 U.S.C. Section 355(a) prohibiting introduction into

(Cont'd)

the drug. The prosecution proceeded and resulted in acquittal, followed by conviction of a juror of criminal contempt for having brought extra-judicial information concerning Krebiozen to the attention of fellow jurors. See United States v. Bukowski, 435 F.2d 1094 (7th Cir. 1970). (c) Tutoki v. Celebrezze, 375 F.2d 105 (7th Cir. 1967). Although present plaintiffs do not appear to have been parties, this court said "The present posture of Krebiozen vis-a-vis the Food and Drug Administration (FDA) is that it is not approved under or exempted from section 505." (d) Rutherford v. American Medical Association, 379 F.2d 641 (7th Cir. 1967), cert. den. 389 U.S. 1043. Again present plaintiffs were not parties. This court said, however, "Krebiozen is unavailable in interstate commerce. As a new drug, it has not received an approval, required by the Food, Drug and Cosmetic Act, 21 U.S.C.A. §355, n.2 which would permit its introduction into interstate commerce." p.643.

interstate commerce of a new drug without an effective NDA.

There appears to be a dispute whether all sales of Krebiozen were expressly restricted by the seller to investigational use. There is room for question concerning the meaning of "commercially" in the grandfather clause. We assume, since Congress was endeavoring to avoid imposing new burdens on drugs which had already achieved "recognized" status, and usage thereunder to a material extent and for a material time, that a gloss of openly and readily available and broadly distributed in the ordinary course of business as well as lack of restriction to investigational use was intended. Nevertheless we find it impossible to say, on the record presented, that defendants conclusively established that Krebiozen was not "commercially used or sold" as of October 9, 1962.

Grandfather requirement (B): "generally recognized as safe" as of October 9, 1962.

Defendants presented affidavits which, at least prima facie, established (1) that as of the critical date Krebiozen was not generally recognized among qualified experts as safe and effective for management of malignant tumors, and (2) that as of the critical date its composition was not sufficiently known to be recognized as safe in the sense of non-toxic, for use in such treatment.

One affiant was Jesse L. Steinfeld, M.D., Surgeon General, United States Public Health Service. He described his professional background and attainments, much of them in the field of cancer research, and stated

that he is well acquainted with the opinions of experts in the field of cancer, especially chemotherapy, and with the relevant literature and that he is well acquainted with Krebiozen.

Dr. Steinfeld stated: "I know of no medical school which teaches, or has taught, that Krebiozen is a treatment of cancer. I know of no hospital associated with a medical school where Krebiozen is used for treatment of cancer. I know of no expert in the field of cancer who believes now, or who has ever believed, that Krebiozen is safe for the treatment of cancer or that Krebiozen has any efficacy whatsoever in the treatment of cancer . . . . In 1963, I was a member of a committee of twenty-four cancer experts, selected from throughout the United States by the Director of the National Cancer Institute, who evaluated data on 504 patients submitted by Krebiozen's sponsors. I personally reviewed thirty-nine of the cases and participated in the review of many of the others. The Committee unanimously concluded that there was no substantive evidence in the data to demonstrate that Krebiozen was of any value whatsoever in treating cancer . . . . Based on my professional education, training, and experience, on my knowledge of published scientific literature, and in my contact with colleagues, it is my opinion that the composition of Krebiozen is such that I do not recognize it, nor is it generally recognized by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe or effective when used for the treatment of cancer in the manner suggested in its labeling. The drug has never been so recognized."

Opinion

Another affiant was Carl G. Baker, M.D., Director, National Cancer Institute, United States Public Health Service. He described his professional background and attainments, and substantial experience and expertise in the field of cancer, especially in the area of chemotherapy. He asserted similar opinions with respect to general recognition of Krebiozen.

With respect to the lack of general knowledge of the composition of Krebiozen as of October 9, 1962, Dr. Steinfeld and Dr. Baker each stated as follows:

"The actual composition of Krebiozen was not known to any expert in the field of cancer until 1963, when the Department of Health, Education, and Welfare released information concerning assays of the drug's composition. To my knowledge no meaningful scientific bioassay data on Krebiozen has ever been available to experts. Experts in the field of cancer, lacking information about a drug's composition or about its biological activity, could not have made a determination prior to 1963 concerning the safety of this drug."

Plaintiffs submitted the affidavits of Andrew C. Ivy, M.D. and Marko Durovic. Although they presented material to support a claim that Krebiozen is thought by some physicians to be safe and effective in the treatment of cancer, they by no means asserted that it is generally so recognized among experts.

Dr. Ivy described his very impressive qualifications and experience as a physician, teacher and author. He asserted that he had studied Krebiozen in collaboration with plaintiff Stevan Durovic, had treated hundreds of

patients with Krebiozen and "analyzed and reviewed the observations and experiences of more than 3,000 licensed physicians who have treated about 4,227 patients, most of whom were afflicted with advanced or hopeless cancer." He asserted that Krebiozen is non-toxic, that it "is a tissue hormone, which functions and an anti-cancer substance." He asserted changes observed or reported in large numbers of the patients referred to. He concluded: "In my opinion, as an acknowledged expert on cancer and on Krebiozen, and based upon my own personal experiences and the experience of some 3,000 licensed physicians whose results have been studied by me, Krebiozen is safe and beneficial in the treatment of cancer, and possesses significant palliative, arresting and remissive action on human cancer."

Plaintiff Durovic asserted no medical nor scientific qualifications. His affidavit was divided into eight parts, as follows:

1. "Krebiozen is not creatine." (HEW has at times, beginning in September 1963, announced that ampules of Krebiozen contain mineral oil and some but not all contain a readily available and inexpensive laboratory substance known as creatine.) Affiant stated that creatine monohydrate is an impurity, associated in the ampule with a yellowish material or oil, a complex structure the components of which would require 10 years of effort to identify. He asserted that in the criminal trial it had been proved that Krebiozen was not mere creatine monohydrate, and referred to the testimony of various witnesses on that issue.

2. "Krebiozen is effective in the treatment of cancer." Affiant asserted what he considered inadequacies in the qualifications, procedure, and standards of the committee of 24 referred to by Dr. Steinfeld.

3. "Krebiozen is effective in the treatment of advanced and hopeless cancer cases." Affiant stated that a hospital in Philadelphia and a number of physicians have treated patients with Krebiozen. He summarized or related certain testimony of Dr. John Pick who had seen cancer patients experience favorable results after treatment with Krebiozen and who stated that "it is of great help in the management of cancer."

4. "The Affidavit of Marion I. Finkel, M.D., Deputy Director Bureau of Drugs of FDA." Affiant pointed out that this affidavit, asserting certain announcements by FDA, did not establish the announcements were true.

5. "The Affidavit of Joseph Levine." Affiant asserted certain facts which he said renders Levine's determination of the composition of Krebiozen inadequate.

6. "The Affidavits of Dr. Jesse L. Steinfeld and Dr. Carl G. Baker." Affiant asserted various facts on the basis of which he said their affidavits lack probative value.

7. "The Affidavits of Levine, Finkel, Baker, and Steinfeld." Affiant asserted Dr. Scott Anderson and Dr. Walter McCrone had established that Krebiozen was not creatine monohydrate, and that in the criminal trial defendants were acquitted because of the government's

failure to prove that Krebiozen is creatine monohydrate or that ampules labeled Krebiozen and containing mineral oil, lacked Krebiozen powder.

8. "Krebiozen is safe and not toxic." Affiant stated that Krebiozen is not toxic, and that this was proved by statements of physicians who had administered thousands of injections, Dr. Ivy's observations, Dr. Pick's testimony that he had been injected with 100 ampules without ill effects, and the report to that effect of the Philadelphia hospital after treating 40 patients.

It must be remembered that the issue presented under the applicable law is not whether Krebiozen is in fact non-toxic, nor in fact effective, nor whether some physicians or experts could be found who considered it so, but solely whether by October 9, 1962, it had achieved general recognition among the experts as safe for the management of malignant tumors, as the term "safe" was then properly interpreted.[4] It is clear that neither Dr. Ivy's affidavit nor the reports and opinions of others, reported by Durovic's affidavit, purported to assert that Krebiozen had, as of October 9, 1962, achieved general recognition among experts as safe or safe and effective.

Analytically, it is plausible to argue that the addition by Congress of "effective" to the standard by which drugs were to be judged on and after October 10, 1962, meant that effectiveness was not part of the

4. United States v. Seven Cartons, More or Less, etc., 424 U.S. 1364 (7th Cir. 1970); Tyler Pharmacal Distrib. Inc. v. U.S. Dept. of Health, E. & W., 408 F.2d 95, 99 (7th Cir. 1969); AMP Incorporated v. Gardner, 389 F.2d 825, 831 (2d Cir. 1968).

standard before that date, when only "safe" appeared. On the other hand, it is clear that those responsible for the change understood that "The Food and Drug Administration now requires, in determining whether a 'new drug' is safe, a showing as to the drug's effectiveness where the drug is offered for use in the treatment of a life-threatening disease .... In such cases, the determination of safety is, in the light of the purposes of the new drug provisions, considered by the Food and Drug Administration to be inseparable from consideration of the drug's effectiveness. The provisions of the bill are in no way intended to affect any existing authority of the Department of Health, Education, and Welfare to consider and evaluate the effectiveness of a new drug in the context of passing upon its safety." [5]

The thinking behind the position referred to is illustrated in the Steinfeld and Baker affidavits, as follows: "The use of an ineffective drug such as Krebiozen for the treatment of a life-threatening disease such as cancer is not a safe medical practice. Any delay in the institution of effective therapy (e.g., radiation, surgery, effective chemotherapy) caused by the use of an ineffective drug allows the disease to progress beyond control. Delay means almost certain death."

Bearing in mind the weight properly accorded to administrative construction, and Congressional awareness of the administrative view that the concept of safety in the law before the 1962 amendments included the concept of effectiveness for its indicated use where the drug is offered for use in the treatment of life-threatening disease, we think the definition of new drug before the amendments should be construed

5. Senate Report No. 1744, July 19, 1962, 1962 U.S. Code Congressional and Administrative News, p. 2891.

accordingly. It would follow that a drug offered for use in the treatment of cancer is now, and was before the amendments, a new drug unless it has achieved general recognition among the experts as safe and effective for such use.

Under that analysis, the status of a drug offered for such use would be subjected to the same test before and after the amendments, and the grandfather clause would have no effect on it. [6]

Applying the reasoning just stated, the declaratory judgment was clearly correct. The affidavits demonstrate, beyond any issue of fact, that Krebiozen has not, either before or after October 9, 1962, achieved general recognition among qualified experts as safe and effective for use in the management of malignant tumors.

If, however, we are in error in such reasoning, an alternative path also leads us to affirm the judgment. Assuming arguendo that even for drugs intended for treatment of life-threatening disease, "safe," before the 1962 amendments, meant only non-toxic, the affidavits have established that, as of October 9, 1962, the identity and composition of Krebiozen was so completely unknown that it could not, for that reason, have been generally recognized among qualified experts as safe, even in the narrow sense, for its indicated use.

We have been made aware, in this record, of much of the emotionally charged controversy about Krebiozen. Some characterize Krebiosen as a hoax, yet there are many who believe with deep sincerity that a

6. In any event a grandfather clause exception is to be construed strictly against one who invokes it. United States v. Allan Drug Corporation, 357 F.2d 713, 718 (10th Cir. 1966) cert. den. 385 U.S. 899.

number of cancer sufferers have been aided, or even saved, by it. Its advocates contend that the medical "establishment" both in and out of government has unfairly denied Krebiozen a reasonable test. So distinguished a person as the Honorable Paul Douglas, former Senator from Illinois, has taken its part. Some would argue that if a substance is found to be innocuous, a sufferer who hopes it will relieve him is entitled to have it.

The issues suggested by the last paragraph, however, are not before us for decision.

The law, as Congress enacted it, looks primarily to the administrative process for deciding which new drugs meet appropriate standards for introduction into interstate commerce. That process is to protect the public through granting, denying, and suspending the effectiveness of NDA's. Administrative decisions are subject to judicial review, within the appropriate limits. Realizing, however, that there were already on the market, or might come to be, drugs offered to the public which already were, or would be, so clearly recognized as safe (before the 1962 amendments) or as safe and effective (thereafter) that subjecting them to the administrative process would be unnecessary and wasteful, Congress allowed them to bypass the NDA procedure. We think the standard of general recognition by qualified experts was intended to be strictly construed so that unless a drug is clearly entitled to proceed through the direct channel, it must proceed through the NDA channel.

Opinion

Interpreting the law in the light of its purpose[7] we are convinced that neither as of October 9, 1962, nor since, has Krebiozen achieved the extent and type of general recognition that entitles a drug to short-circuit the NDA procedure.

The judgment appealed from is affirmed.

A true Copy:

Teste:

Clerk of the United States Court of
Appeals for the Seventh Circuit

7. United States v. Dotterweich, supra, fn. 1, p. 280.

Order of United States District Court for the Northern District of Illinois

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

MARKO DUROVIC, an individual and also known as MARKO DUROVIC, formerly d/b/a DUGA LABORATORIES: STEVAN DUROVIC, d/b/a PROMAK LABORATORIES and KREBIOZEN RESEARCH FOUNDATION, a corporation,

Plaintiffs,

v. No 69 C 32

ELLIOT RICHARDSON, Secretary of Health, Education & Welfare, and CHARLES C. EDWARDS, Commissioner of Food & Drugs,

Defendants,

This cause having come before the Court on cross motions for summary judgment pursuant to Rule 56 of the Federal Rules of Civil Procedure, and the Court having considered the pleadings, answers to interrogatories, memorandums and affidavits of the parties, and having filed findings of fact and conclusions of law, it is hereby

ORDERED, ADJUDGED AND DECREED that Defendants' Motion for Summary Judgment is granted and Plantiffs' Motion for Summary Judgment is denied; and it is further

Order

ORDERED, ADJUDGED AND DECREED that Krebiozen is now and has always been a new drug within the meaning of the statutory definition for which no approved New Drug Application is now or has ever been effective; and it is further

ORDERED, ADJUDGED AND DECREED that the complaint is dismissed.

ENTER:

J.S. Perry
JUDGE

DATED: May 18, 1971

Finding of Facts and Conclusions of Law of United States District Court of Northern District of Illinois

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

MARKO DUROVIC, an individual and also known as MARKO DUROVIC, formerly d/b/a DUGA LABORATORIES: STEVAN DUROVIC, d/b/a PROMAK LABORATORIES and KREBIOZEN RESEARCH FOUNDATION, a corporation,

Plaintiffs,

v.

ELLIOT RICHARDSON, Secretary of Health, Education & Welfare, and CHARLES C. EDWARDS, Commissioner of Food & Drugs,

Defendants.

1. Plaintiffs filed a Complaint for Declaratory Judgment pursuant to Title 28, United States Code, Sections 1337 and 2201 seeking to have this Court determine that their drug Krebiozen is not a new drug within the meaning of the Federal Food, Drug and Cosmetic Act and is exempt from complying with the new drug provisions of the Act by virtue of the grandfather clause, section 107(c)(4) of the Drug Amendments of 1962. In the alternative, the Complaint seeks to have this Court determine that their drug Krebiozen has the status of a new drug for which new drug applications become effective on June 15, 1954

with respect to New Drug Application No. 9368 and on June 12, 1961 with respect to New Drug Application No. 12-823.

2. The defendants answered the Complaint and alleged that Krebiozen has always been a new drug within the meaning of the Act, that the grandfather clause is not applicable, that no New Drug Application has been approved or became effective, and that Krebiozen cannot be introduced into interstate commerce until the new drug provisions of the Act have been satisfied.

3. Labeling and other promotional material establish that Krebiozen is a drug intended to be used in the management and treatment of malignant tumors.

4. Both parties have filed a motion for summary judgment pursuant to Rule 56 of the Federal Rules of Civil Procedure.

5. The defendants submitted the affidavits of two medical experts: Jesse L. Steinfeld, M.D., Surgeon General of the United States and Deputy Assistant Secretary for Health and Scientific Affairs, Department of Health, Education and Welfare; and Carl G. Baker, M.D., Director of the National Cancer Institute, National Institutes of Health.

6. The affidavits of Dr. Steinfeld and Dr. Baker establish that there is no general recognition, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that Krebiozen is now or has ever been safe or effective for the management or treatment of malignant tumors.

Finding of Facts and Conclusions

7. The affidavits and other evidence submitted by plaintiffs do not controvert the affidavits of Dr. Steinfeld and Dr. Baker.

8. The defendants also submitted the affidavit of Marion J. Finkel, M.D., Deputy Director, Bureau of Drugs, Food and Drug Administration, United States Department of Health, Education and Welfare. Dr. Finkel's affidavit establishes that the Food and Drug Administration has never approved a New Drug Application for Krebiozen; that the new drug applications for Krebiozen submitted to the Agency on April 15, 1954 (New Drug Application No. 9368) and April 13, 1961 (New Drug Application No. 12-823) were not accepted for filing because they were incomplete and inadequate; and that the applicants were notified of this decision within sixty days after each New Drug Application was received by the Agency.

CONCLUSIONS OF LAW

1. This Court has jurisdiction over the parties and subject matter.

2. Krebiozen is now and has always been a new drug within the meaning of the statutory definition.

3. Krebiozen is not protected by the grandfather clause, section 107(c)(4) of the Drug Amendments of 1962.

4. No approved New Drug Application is now or has ever been effective with respect to Krebiozen.

Finding of Facts

5. Krebiozen cannot be introduced or delivered for introduction into interstate commerce until a New Drug Application filed pursuant to Title 21, United States Code, Section 355(b) is approved and made effective.

6. There is no genuine issues of material fact precluding judgment, and the Government is entitled to judgment as a matter of law.

7. The Government's motion for summary judgment is granted, and the summary judgment motion of plaintiff is denied.

Let judgment be entered accordingly.

ENTER:

J. S. Stern
STERN

DATED: May 18, 1971

Fifth Amendment of the United States Constitution

No person shall be held to answer for a capital, or otherwise infamous crime, unless on a presentment or indictment of a Grand Jury, except in cases arising in the land or naval forces, or in the Militia, when in actual service in time of War or public danger; nor shall any person be subject for the same offence to be twice put in jeopardy of life or limb; nor shall be compelled in any criminal case to be a witness against himself, nor be deprived of life, liberty, or property without due process of law; nor shall private property be taken for public use, without just compensation.

Administrative Procedure Act 5 Sections 701 - 704

SECTION 701. Application; definitions

(a) This chapter applies, according to the provisions thereof, except to the extent that—

(1) statutes preclude judicial review; or

(2) agency action is committed to agency discretion by law

(b) For the purpose of this chapter—

(1) "agency" means each authority of the Government of the United States, whether or not it is within or subject to review by another agency, but does not include—

(A) The Congress;

(B) the courts of the United States;

(C) the governments of the territories or possessions of the United States;

(D) the government of the District of Columbia

(E) agencies composed of representatives of the parties or of representatives of organizations of the parties to the disputes determined by them;

(F) courts martial and military commissions;

(G) military authority exercised in the field in time of war or in occupied territory; or

(H) functions conferred by sections 1738, 1739, 1743, and 1744 of title 12; chapter 2 of title 41; or sections 1622, 1884, 1891-1902, and former section 1641(b)(2), of title 50, appendix; and

(2) "person", "rule", "order", "license", "sanction", "relief", and "agency action" have the meanings given them by section 551 of this title.

Pub. L. 89-554, Sept. 6, 1966, 80 Stat. 392.

SECTION 702. Right of review

A person suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action within the meaning of a relevant statute, is entitled to judicial review thereof. Pub. L. 80-554, Sept. 6, 1966, 80 Stat. 392.

SECTION 703. Form and venue of proceeding

The form of proceeding for judicial review is the special statutory review proceeding relevant to the subject matter in a court specified by statute or, in the absence or inadequacy thereof, any applicable form of legal action, including actions for declaratory judgments or writs of prohibitory or mandatory injunction or habeas corpus, in a court of competent jurisdiction. Except to the extent that prior, adequate, and exclusive

opportunity for judicial review is provided by law, agency action is subject to judicial review in civil or criminal proceedings for judicial enforcement. Pub. L. 89-554, Sept. 6, 1966, 80 Stat. 392.

SECTION 704. Actions reviewable

Agency action made reviewable by statute and final agency action for which there is no other adequate remedy in a court are subject to judicial review. A preliminary, procedural, or intermediate agency action or ruling not directly reviewable is subject to review on the review of the final agency action. Except as otherwise expressly required by statute, agency action otherwise final is final for the purposes of this section whether or not there has been presented or determined an application for a declaratory order, for any form of reconsideration, or, unless the agency otherwise requires by rule and provides that the action meanwhile is inoperative, for an appeal to superior agency authority. Pub.L. 89-554, Sept. 6, 1966, 80 Stat. 392.

Pertinent Provisions of the Federal Food, Drug & Cosmetic Act of 1938, 21 U.S.C. Section 301 Et Seq

Title 21 U.S.C. 321(p) (current) provides as follows:

(p) The Term "new drug" means —

(1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this Act it was subject to the Food and Drugs Act of June 30, 1906, as amended and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

Title 21 U.S.C. 321(p), prior to Oct. 10, 1962, provided as follows:

(p) The term "new drug" means —

(1) Any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this Act it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use, or

(2) Any drug the composition of which is such that such drug, as a result of investigations to determine its safety for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

Title 21 U.S.C. 355 (current), provides as follows:

Section 355. New drugs—Necessity of effective approval of application

(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug.

Pertinent Provisions

Filing application; contents

(b) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (1) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (2) a full list of the articles used as components of such drug; (3) a full statement of the composition of such drug; (4) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (5) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (6) specimens of the labeling proposed to be used for such drug.

Title 21, U.S.C. 355, prior to Oct. 10, 1962, provided as follows:

Section 355. New drugs—Necessity of effective application

(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an application filed pursuant to subsection (b) of this section is effective with respect to such drug..

controls used for, the manufacture, processing, and packing of such drug; (5) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (6) specimens of the labeling proposed to be used for such drug.

Filing application; contents

(b) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (1) full reports of investigations which have been made to show whether or not such drug is safe for use; (2) a full list of the articles used as components of such drug; (3) a full statement of the composition of such drug; (4) a full description of the methods used in, and the facilities and

Section 335. Hearing before report of criminal violation

Before any violation of this chapter is reported by the Secretary to any United States attorney for institution of a criminal proceeding, the person against whom such proceeding is contemplated shall be given appropriate notice and an opportunity to present his views, either orally or in writing, with regard to such contemplated proceeding.

June 25, 1938, c. 675, Section 305, 52 Stat. 1045; 1940 Reorg. Plan No. IV, 12, eff. June 30, 1940, 5 F.R. 2422, 54 Stat. 1237; 1953 Reorg. Plan No. 1, Section 5, eff. Apr. 11, 1953, 18 F.R. 2053, 67 Stat. 631.

Section 107 (c) of the Drug Amendments of 1962 (Including the "Grandfather" Clause)

Clause, Section 107 (c) (4), 76 Stat 489)

(c) (1) As used in this subsection, the term "enactment date" means the date of enactment of this act; and the term 'basic Act' means the Federal Food Drug, and Cosmetic Act [this chapter].

(2) An application filed pursuant to section 505 (b) of the basic Act [section 355 (b) of this title] which was 'effective' within the meaning of that Act on the day immediately preceding the enactment date shall be deemed as of the enactment date to be an application 'approved' by the Secretary within the meaning of the basic Act as amended by this Act.

(3) In the case of any drug with respect to which an application filed under section 505 (b) of the basic Act is deemed to be an approved application on the enactment date by virtue of paragraph (2) of this subsection—

(A) the amendments made by this Act to section 201(p), and to subsections (b) and (d) of section 505, of the basic Act [subsec. (p) of this section, and subsecs. (b) and (d) of section 355 of this title, insofar as such amendments relate to the effectiveness of drugs, shall not, so long as approval of such application is not withdrawn or suspended pursuant to section 505(e) of that Act [section 355(e) of this title], apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling covered by such approved

application, but shall apply to any changed use, or conditions of use, prescribed, recommended, or suggested in its labeling, including such conditions of use as are the subject of an amendment or supplement to such application pending on, or filed after, the enactment date; and

(B) clause (3) of the first sentence of section 505(e) of the basic Act, as amended by this Act [section 355(e) of this title], shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling covered by such approved application (except with respect to such use, or conditions of use, as are the subject of an amendment or supplement has been approved after the enactment date under section 505 of the basic Act as amended by this Act [section 355 of this title]) until whichever of the following first occurs: (i) the expiration of the two-year period beginning with the enactment date; (ii) the effective date of an order under section 505 (e) of the basic Act [section 355 (e) of this title], other than clause (3) of the first sentence of such section 505 (e) [section 355 (e) of the title], withdrawing or suspending the approval of such application.

(4) In the case of any drug which, on the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force

Section 107 (c) of the Drug Amendments of 1962

[subsec. (p) of this section], and (c) was not covered by an effective application under section 505 of that Act [section 355 of this title], the amendments to section 201(p) of this section] made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day."

Affidavit of Andrew C. Ivy, M. D.

UNITED STATES DISTRICT COURT NORTHERN DISTRICT OF ILLINOIS EASTERN DIVISION

MARKO DUROVIC, an individual, and also as MARKO DUROVIC, formerly d/b/a DUGA LABORATORIES: STEVAN DUROVIC, d/b/a PROMAK LABORATORIES; and KREBIOZEN RESEARCH FOUNDATION, a corporation,

Plaintiffs,

v.

ELLIOTT CHARDSON, Secretary of Health, Education, and Welfare, and CHARLES C. EDWARDS, Commissioner of Food and Drugs,

Defendants.

Civil Action No. 69C32

STATE OF ILLINOIS
COUNTY OF COOK

ANDREW C. IVY, M.D., being first duly sworn, deposes and says:

Affidavit

I submit this affidavit in this action not as an advocate for or against either party, but merely to give the Court the benefit of my opinion as to the safety and benefit of Krebiozen based upon years of personal experience with the drug.

I am a physician, Professor Emeritus of the University of Illinois, College of Medicine, former Executive Director of the National Advisory Cancer Council of the U.S. Public Health Service, and former member of the Board of Directors of the American Cancer Society. I have written and published and collaborated in writing more than 1,500 scientific papers, books, monographs, studies and articles. Thirty-five publications are in the field of cancer with Krebiozen to wit: "Krebiozen an Agent in the Treatment of Cancer, 1951"; "Observations on Krebiozen in the Treatment of Cancer, 1956"; "Action of Krebiozen on Tumors in Dogs and Cats, 1961"; and "Krebiozen Theory, Toxicity and Observation in Animal and Human Patients with Cancer, 1961."

I have discovered and helped to establish the existence of five hormones in the body.

I was Consultant and a Witness at the Nuremberg Tribunal on War Crimes of a Medical Nature, serving the U.S. and World Medicine on the subject of Medical Ethics, Medical Science and Human Rights. I am the author of the Nuremberg Code for the conditions under which humans may serve as subjecs in medical experiments. I have taught more than 5,500 medical students in the areas of physiology, pathology, pharmacology, the treatment of diseases and Materia Medica, Toxicology, the Anatomy and Physiology of the Signs and Symptoms of Diseases.

Affidavit

There is attached to this affidavit a copy of my curriculum vitae listing my education, employment and other activities, my honorary degrees, special recognitions and my honorary memberships in Medical Societies and Academies throughout the world.

In August of 1949, in collaboration with Dr. Steven Durovic and other physicians, I started making observations and studies on the effect of Krebiozen in animals and in human patients with advanced cancer, upon whom all indicated treatment had been tried without beneficial effect.

In the course of my work with Krebiozen since 1949 I treated hundreds of patients alone and in collaboration with other distinguished colleagues and have also analyzed and reviewed the observations and experiences of more than 3000 licensed physicians who have treated about 4227 patients, most of whom were afflicted with advanced or hopeless cancer.

Krebiozen is non-toxic. Absence of acute or accumulative toxicity was reported in 65 cogs, 135 rats, 284 mice, 4 guinea pigs, 2 cats, 3 scientists (Drs. Ivy, Krasno, and Durovic before administrating the drug on patients, injected themselves) and as reported with respect to the report discussed above with 4227 patients. Mild local irritation at the site of injection may occur in approximately 5% of the patients as a result of the mineral oil. However, this reaction is not seen when Krebiozen is dissolved in aqueous solution or sunflower oil. If the site is massaged several times a day, the occurrence of this local irritation disappears or is adequately controlled.

Affidavit

The site of primary tumor or its metastases, on whom observations on change is size were reported, was observed in 2934 of the patients. During the first three months after Krebiozen administration, the tumor or metastases decreased in size in 36% of the patients and was arrested in 52% of the patients.

Of 4194 patients 85% or 3552 patients had pain. 64% of these reported a complete or partial reduction in pain during the first 3 months after the start of Krebiozen. In some tumor types, the relief amounted to 77%, in others only 32%.

On the basis of analysis of reports on approximately 4227 patients made by approximately 3300 physicians, including my own experience in treatment of hundreds of patients personally, I have concluded that Krebiozen possesses a significant palliative, arresting and remissive action on human cancer, more so for some cancer types than for other cancer types.

Krebiozen is a tissue hormone, which functions and an anti-cancer substance. This was first established by the affiant in 1951, and from 1961 to 1963 this theory was confirmed by five different groups of scientists in the United States. The affiant found it to be active in both animal and human patients.

In my opinion, as an acknowledged expert on cancer and on Kreiozen, and based upon my own personal experiences and the experience of some 3000 licensed physicians whose results have been studied by me, Krebiozen is safe and beneficial in the treatment of

cancer, and possesses significant palliative, arresting and remissive action on human cancer.

s/Andrew C. Ivy, M.D.
ANDREW C. IVY, M.D.

Sworn to before me this

30th day of March, 1971

s/Catherine A. Barbaro
NOTARY PUBLIC

Affidavit

PERSONAL

Born: Farmington, Missouri; February 25, 1893.

Parents: Henry McPherson and Cynthia (Smith) Ivy.

Married: Emma Anna Kohman, December 24, 1919.

Children: John Henry, William Harvey, Andrew Conway, Horace Kohman, Robert Emerson.

Religion: Methodist.

Home Address: 8158 South Merrill Avenue, Chicago 17, Illinois.

Office Address: Roosevelt University, 430 South Michigan, Chicago 5, Illinois.

Biographies appear: Who's Who in America, International Who's Who, Who's Who in Medicine, American Men of Science*, Who's Who in American Education, Leaders in Education, Biographical Encyclopedia of the World, The List of Society, International Year Book and Statesmen's Who's Who and Who's Who in the Mid West.

EDUCATION

A.B., B.Pd., State Normal School, Cape Girardeau, Mo., 1913.

B.S. (1916), M.S. (1917), Ph.D. (1918), University of Chicago.

Affidavit

M.D. Rush Medical College, 1911.

Internship, Mercy Hospital; Augustana Hospital, Chicago, 1921-22.

Licensed to practice medicine and surgery, State of Illinois, 1922.

HONORARY DEGREES

D.Sc. University of Nebraska, 1947.
D.Sc. Grinnell College (Iowa), 1947.
D.Sc. Boston University, 1948.
D.Sc. Hastings College, 1951.
LL.D. Loyola University (Chicago), 1950.
D.Sc. Coe College (Iowa), 1951.

SPECIAL RECOGNITIONS

Distinguished Alumni Award, University of Chicago, 1941.

Pope Leo XIII Award for Outstanding Contributions to Humanity by Bishop Shell School of Social Studies, 1953.

Eloy Alfaro Decoration for Contributions to the Education of Latin American Students 1953.

Carpenter Medalist of the American Roentgen Ray and Radium Society, 1946.

Distinguished Service Award of the American Congress of Physical Medicine, 1947.

Presidential Certificate of Merit for Outstanding Fidelity and Meritorious conduct in World War II, 1948.

Distinguished Service Award of the National Society for Medical Research, 1953.

SPECIAL RESEARCH AWARDS

American Medical Association Gold Medal for Research on the Experimental Production of Intersexuality, 1938.

American Medical Association Gold Medal for Research on the Formation of Bile, 1941.

American Medical Association Silver Medal for Research on the Effect of Caffeine on the Stomach, 1944.

American Medical Association Bronze Medal for Research on Flicker Photometry and Cardiovascular Disease, 1950.

American Medical Association Medal for Exhibition Anatomy and Physiology of Child Birth.

HONORARY MEMBER OF MEDICAL SOCIEITIES

Harvey Society, New York City.
National Academy of Medicine,
Buenos Aires, Argentina.
American Academy of General Practice.
Chicago Orthodontographic Society.
Des Moines Academy of Medicine.
Gorgas Medical Society Fellow.
St. Louis County Medical Society.
Tacoma Surgical Socity.

Affidavit

TEACHING AND RESEARCH POSITIONS

Instructor in Physiology, University of Chicago, 1917-19.

Associate Professor of Physiology, Loyola University School of Medicine, Chicago, 1919-23.

Associate Professor of Physiology, University of Chicago, 1923-25.

Nathan Smith Davis Professor of Physiology and Pharmacology and Head of the Division of Physiology and Pharmacology, Northwestern University Medical School, 1925-46.

Scientific Director, Naval Medical Research Institute, Bethesda, Maryland, 1942-43.

Vice-President of the University of Illinois in charge of the Chicago Professional Colleges, 1946-53.

Distinguished Professor of Physiology and Head of the Department of Clinical Science, 1946-1961.

Distinguished Professor Emeritus University of Illinois, 1962 to .

Research Professor of Biochemistry, Roosevelt University, and Director of the Medical Research Laboratory, 1963 .

PHILOSOPHICAL CONTRIBUTIONS

Affidavit

Some Ethical Implications of Science: Has Science an Ethic? (Illinois Science Teachers, Assoc. Address Roosevelt University).

The Ethics of Experiments on Human Beings: (Convocation: Soc. Experimental Biology and Medicine)

Medical Research - Operation Humanity

Representing Medical Science at the Centennial of the American Association for Advancement of Science

The Meaning of a Liberal Education. Convocation Address American College of Surgeons.

Literacy For What. Convocation Address at the University of Chicago.

The Meaning of the Heart of the Declaration of Independence. Address - Coe College Convocation.

Epilogue: The Evidence of God in an Expanding Universe.

Discrimination In Higher Education. In Public Opinion Pamphlet Series No.153, (1949).

GENERAL AND CIVIC CONTRIBUTIONS

Cofounder of the Research Foundation for the Eradication of Tuberculosis by BCG Vaccination.

Cofounder and President of the Chicago Committee for the Rehabilitation of Alcoholics.

Affidavit

Cofounder and President of the International Commission for the Prevention of Alcoholism Through Edcuation.

Cofounder and Secretary of the National Society for Medical Research.

Vice - Deputy Director of the Chicago Civil Defense Organization.

Consultant and Witness at the Nuremberg Tribunal on War Crimes of a Medical Nature Serving the U.S. and World Medicine on the Subjects of Medical Ethics, Medical Science, and Human Rights. Author of the Nuremberg Code for the conditions under which humans may serve as subjects in medical experiments.

Cofounder and President of the National Conference of Educators to eliminate through education, discriminations in higher education on the basis of religion, creed, color and economic position.

As Vice-President of the University of Illinois Dr. Ivy was instrumental in raising funds to the extent of more than $45,000,000 for medical buildings in the West Side Medical Center of Chicago, and for Residences and a Community Steam Plant.

CONTRIBUTIONS W.W.I.

(a) Prior to the War he was a Lieutenant in the Missouri National Guard.

(b) During the War he was directed to teach the Principles of Surgical Operations on the Brain and Spinal Cord to U.S. Army Surgeons.

Affidavit

CONTRIBUTIONS TO WORLD WAR II.

1. Developed a Welders Mask for workers in closed spaces as tanks.

2. Free Fall from 32,000 ft. altitude.

3. The two-flap oxygen mask.

4. Explosive decompression.

5. Dr. Ivy trained 24 physicians to perform Research in the American Air Force and to teach pilots of the dangers of high altitude.

6. Four of the 24 received Presidential Legion of Merit Awards.

7. Dr. Ivy was a cofounder of the Society for Space Medicine.

NAVAL MEDICAL RESEARCH INSTITUTE, BETHESDA, MARYLAND, WORLD WAR II.

1. Desalination of sea water. (Dehydrated himself 3 times to the point of hallucinations, and developed gall stones as a result.)

2. Minimal water requirements.

3. Toxicity of sea water.

4. Antiflashburn cream.

5. Sterilization of canteen water.

6. Pressure breathing of oxygen at high altitudes.

7. New treatment of athletes foot.

8. Treatment of Scrub Typhus.

9. Dried blood plasma and influenze virus.

10. Medical treatment of acute appendicitis.

11. Dr. Ivy and his colleagues tested an antifatigue drug on the performance of cross-country truck drivers and on the marksmanship of Marine soldiers kept marching day and night for 3 days. This antifatigue drug was also tested on some 5,000 soldiers and found to be non-toxic when used in doses which decrease fatigue. The use of drug was made a command decision in the Army during World War II.

FURTHER CONTRIBUTIONS WORLD WAR II.

He and his colleagues showed that the slight oxygen lack, as occurs above an altitude of 5,000 [illegible] decreases mental and motor abilities.

13. Naval Medical Research Institute, [illegible], Md., Scientific Director, 1942-43; Consultant, [illegible].

14. U.S. Navy, Member of Board of Medical Consultants to Surgeon General, 1946-52.

15. U.S. Army, Quartermaster General, Consultant, Planning Division, 1943-44; Research and Development Branch, 1943-46.

16. U.S. Army, Office of the Surgeon General, Consultant, Nutrition Laboratory, 1944-46.

17. National Advisory Cancer Council, Executive Director, 1947-51, member, 1944-51.

18. National Research Council, member, Committee on Nutrition of Industrial Workers, 1944-47; Subcommittee on Clinical Investigation, 1940-45; Sub-Committee on Depression Sickness, 1941-45

19. Advisory Committee to State of Illinois, Chariman, Division of Correction, 1947.

20. State of Illinois Advisory Council on Hospitals, member, 1946-47.

21. Special Committee for Improvement of Cook County Institute (Cook County Special Hospital, Oak Forest Infirmary, Juvenile Detention Home), 1947.

22. Psychiatric Council, Department of Public Welfare, State of Illinois, 1950-54.

23. Medical Center Commission, Member, 1951-54.

SCIENTIFIC CONTRIBUTIONS

1. Dr. Ivy started teaching in 1911 when he was 18 years old. As a teacher in high school and a coach of athletics he saved money to study medicine.

2. He has taught more than 5500 medical students the subjects of:

Physiology,

Affidavit

Pathology,
Pharmacology,
The treatment of Diseases and Materia Medica, Toxicology,
The Anatomy and Physiology of the Signs and Symptoms of Disease.

3. Over 300 young men and women have done research under Dr. Ivy and have received the Master of Science or Dr. of Philosophy degree. These students are teaching medicine: in Mexico, Brazil, Peru, Argentina, Japan, China, Formosa, India, South Africa, Egypt, Greece, Czechoslovakia, Sweden, England, and in several States of the United States.

BOOKS AND MONOGRAPHS

Dr. Ivy and colleagues have published the following books and monographs:

(1) Peptic Ulcer (Gastric and Duodenal Ulcer) Translated into Spanish (1200 pages)
(2) Gastrointestinal Hormones
(3) The Alimentary Tract of Infants and Children
(4) Histamine - A Gastric Hormone
(5) The Gallbladder
(6) Manual for the Treatment of Phosgene Gas Poisoning, used for World War II.

He and his colleagues have published more than 1500 articles.

Dr. Ivy first did research in the field of Experimental Psychology and Education. He studied tests of ability in arithmetic and the rate of learning of short hand and typewriting.

Affidavit

His first medical research proved that drinking moderate amounts of water with and between meals improved the digestion of foods.

He established the medical diagnostic meaning of involuntary movements of the eyes.

He was the first to show that a pouch of the stomach or of the small intestine can be surgically transplanted under the skin. ("Ivy Pouch")

He showed that a blood vessel (carotid artery) could be transplanted from one dog to another as early as 1923.

He demonstrated that the stomach may be completely removed and health maintained by the proper attention to the diet.

He proved that animals may be maintained by intravenous feeding of the proper nutrients.

He discovered how the liver produces balanced quantities of bile salts.

He discovered the cause of heart pain in coronary obstruction.

He, in 1918 to 1924, used X-rays to study the alimentary tract in hunger and after feeding.

He served as a subject sustaining an X-ray bur , which would not heal and had to be removed by surgery.

He found that X-rays irritate body tissues, and does not stimulate them.

He found that human gall stones dissolve when they are placed in the gall bladder of a dog by surgical means.

Sir Howard Florey, who in about 1940 applied the antibiotic penicillin to the treatment of disease in man was a student of Dr. Ivy. Dr. Ivy showed that penicillin could be used to eradicate typhoid germs from the bile passages of human beings. He and his colleagues cleared over 100 typhoid carriers of this condition in an Illinois State Hospital.

He tested the antibiotic streptomicin for toxicity and found that it was the best treatment of lymphogranuloma inguinale.

He served as a consultant in antibiotics from 1944 to 1950.

Dr. Ivy found that obese persons develop a tolerance to anti-appetite drugs after one or two weeks.

Dr. Ivy and his colleagues using human subjects on various diets found how the body regulates its cholesterol balance and that if this balance is upset the cholesterol increases in the lining of the large arteris.

Dr. Ivy and his students developed and showed the greater effectiveness of the "push and pull method", for resuscitation from gas poisoning and drowning.

The "hip-life prone pressure method" is referred to as the "Ivy Method" by some. The "push and Pull"

method has been adopted throughout the World by life-saving agencies.

Dr. Ivy and his colleagues Dr. Gordon, resurrected the Biblical Method of "mouth to mouth" resuscitation, and established its effectiveness and the best way to use the Method.

Dr. Ivy has discovered and established the existence of 5 hormones in the body.

1. Cholecystokinin which causes the gall bladder to contract and evacuate. In the Scandinavian countries, this hormone has been used on more than 75,000 patients for the diagnosis of bile tract complaints.

2. Enterogastrone A which retards the secretion of acid by the stomach.

2. Enterogastrone B which retards spasm of the muscles of the stomach.

3. Enterogastrone B which retards spasm of the muscles of the stomach.

4. Urogastrone A which retards the secretion of acid by the stomach.

5. Urogastrone B which retards the spasm of muscles of the stomach.

He established the existence

(a) of the hormone "gastrin" which stimulates the secretion of acid by the stomach.

(b) of histamine as a gastric hormone.

(c) of secretin as a hormone to stimulate the pancreas to secrete its digestive juice.

(d) of a hunger hormone which causes hunger pains in the stomach.

(c) of a sleep producing substance in the brain when one has been without sleep for 2 or 3 days. This substance has been called "hypnotoxin",

CANCER PUBLICATIONS

1. Gastric Physiology in Relation to Cancer.
Jr. Nat. Cancer Inst., 5:311, 1945.

2. Some Important New & Old Information about Cancer.
What's New, July 1945.

3. Biology of Cancer, Address. Internat. Cancer Congress.
Science 106:2759, 1947.

4. Attempt to Produce Cancer in Gastric Ulcers in Rabbits.
Jr. Nat. Cancer Inst., 7:345, 1947.

5. Thermal Irritation of Alimentary Mucosa.
Federation Proc. 7: March, 1948.

6. Reviews of the Diagnosis and Treatment of Cancer.
Cancer: 1: No. 2, July, 1948.

7. Thermal Irritation and Gastric Cancer.
Cancer, 2:138, 1949.

8. A Cancer Stimulating and Inhibitory Substance in the Liver of Calves.
Report to Lakeland Fndt., Chicago, 1949.

9. Relation of Blood Groups to Pernicious Anemia and Gastric Cancer.
Amer. J. Med. Sci., 217: 194, 1949.

10. Cancer Reasons For Hope.
Address to Second Annual Training School of Amer. Cancer Society, Oct. 27, 1949.

11. Diagnostic Test for Cancer.
Annals Western Med. & Surgery, Sept., 1950.

12. Production of Gastric Cancer Experimentally in a Gastric Ulcer.
Cancer Cancer Research, 10:684, 1950.

13. Cancer Production by over Heated Fat.
Cancer, 3:1044, 1950.

14. Threshold of Pain and Skin Flare of Persons with Malignant Disease.
Amer. J. Physiol., 163:697, 1950.

15. Study of a Serological Test for Cancer.
J. Nat. Cancer Inst., 11:689, 1951.

16. Krebiozen, An Agent for the Treatment of Malignant Tumors.
Champlin-Shealy Co., Chicago, 1951.

17. Skin Flare in Patients with and without Cancer.
J. of Dermatology 19: No. 6, 1952.

18. Lymphosarcoma after feeding Certified Food Dyes.
Cancer Research, 12:309, 1952.

19. The Threshold of Skin Flare in Persons with and Without Malignant Disease.
J. Dermatology, 19: Dec., 1952.

20. Relation of Food Dyes to Cancer.
Gastroenterology, 23:1, 1953.

21. Hepatic Tumors in Rat after Prolonged Feedings of Egg Yolk.
Cancer Research, 14:441, 1954.

22. Cancer Represents the Abnormal Repair of an Injury.
Gastroenterology, 29:199, 1955;

23. Effect of Carcinogens on Gastric Mucosa.
Amer. J. of Physiol., 183:621, 1955.

24. Cause of Gastric Cancer.
Gastroenterology, 28:325, 1955.

25. Effect of Various Irritants in Relation to Gasttic Cancer.

Gastroenterology, 28:345, 1955.

26. Certain Certified Food Dyes Predispose to Cancer.
Exper. Med. & Surgery, 14, 354, 1956.

27. Observations on Krebiozen in the Treatment of Cancer.
Regnery Press, Chicago, 1956.

28. A New Transplantable Sarcoma.
Proc. Amer. Assoc. Cancer Research 2:3, 1957.

29. Destruction of Cancer Cells by Normal Human. Sera.
Exper. Med. & Surgery, 15:300, 1957.

30. Decrease in Resistance to Skin Cancer after Feeding Certain Certified Food Dyes.
Exp. Med. & Surgery, 15:300, 1957.

31. A Transplantable Rat Leiomyo Sarcoma,
Cancer Res., 18:578, 1958.

32. Effect of Human Sera on Cancer Cells.
Proc. 7th, Internat. Cancer Congress, July, 1958.

33. Therapeutic Use of Radioactive Bismuth Isotopes on Malignancy in Man.
Exper. Med. & Surg., 19:9, 1961.

34. Action of Krebiozen on Tumors in Dogs & Cats.

Report to Nat'l. Cancer Inst., Sept., 1961.

35. Krebiozen Theory, Toxicity, and Observations in Animals & Human Patients with Cancer.

Report to Nat'l. Cancer Inst., Sept., 1961.

OTHER ACTIVITIES

American Physiological Society, Secretary 1935-39; President 1939; Member of Editorial Board 1933-34; Board of Publication Trustees, 1933-49; Consulting Editor, 1953—

American Gastroenterology Association, President, 1940-41; member, Editorial Board; Managing Editor, 1942-52.

American Medical Association, Chairman, Section on Physiology and Pathology, 1931-32. Council on Physical Medicine, 1947-51.

Institute of Medicine of Chicago, President, 1944.

Chicago Society of Internal Medicine, President, 1942-43.

Society of Experimental Biology and Medicine, Chairman, Illinois Chapter, 1928-29.

National Society for Medical Research, Secretary-Treasurer, 1946-54.

Affidavit

American Association of University Professors, Council 1929-31.

American Cancer Society, member, Board of Directors, 1946-51.

American College of Physicians, Fellow (Life).

American Institute of Nutrition.

Aero-Medical Association, Space Medicine Association (Charter Member.)

American Association for the Advancement of Science.

American Society for Research in Psychosomatic Problems, 1944-48.

American Institute of Banking, Scientific Advisory Committee, 1946-48.

National Arthritis Research Foundation, Medical and Scientific Advisory Council, 1948-50.

National Foundation for Infantile Paralysis, Inc., General Medical Advisory Committee, Cook County Chapter, 1945-50.

Center Society for Clinical Investigation.

National Society for Crippled Children and Adults, Counselor, 1949-Walter Reed Society.

Illinois Academy of Science.

Commercial Club, Sub-Committee on Medical Plan of Chicago, 1946-48.

Executives' Club, Program Committee, 1947-50.

City Club, Chicago-1952.

University Club, Chicago.

The John Crerar Library, Board of Directors, 1946-

American Red Mogen David for Israel, Inc. Physicians Council.

Vice-Chairman of the Citizens Committee on the Building Code.

Alpha Omega Alpha.

Sigma XI.

Alpha Kappa Kappa.

COMMITTEES AND BOARDS

Research Foundation - Board of Trustees and Vice-President, 1948-

Committee on Cerebral Palsy, Welfare Council of Chicago, 1952-53.

Mayor's Advisory Committee on Allocation of Dogs, 1935-50.

Committee on Vitamin Deficiency Studies, Elgin State Hospital, 1944-48.

Advisory Committee to the Coroner's Office of Cook County, 1946-50.

Mayor's Scientific Advisory Board of Municipal Tuberculosis Sanitarium, 1946-53.

Board of Directors - University of Illinois - Cook County School of Nursing, 1948-54.

Committee on the Establishment of a Chicago Rehabilitation Institute of the Chicago Chamber of Commerce, 1950-53.

Portal House, Chicago Committee on Alcoholism, President, 1951-54.

National Committee for Prevention of Alcoholism, President, 1950-

Annual Reviews, Board of Directors, 1948-52.

International Commission for the Prevention of Alcoholism, President, 1954-62.

Argonne Laboratory, Atomic Energy Research Board, 1947-51.

Committee on Space Medicine (Chairman, 1949) Aero-Medical Association.

Committee on Catastrophic Illness, 1950-52.

Crime Prevention Bureau, Narcotic Committee Chariman, 1950-

Governor's Committee on Ethics for the Use of Prisoners in Medical Experiments, 1948.

Tabulae Biolgicae, Board of Editors 1945.

Hematology Research Foundation, Board of Directors, 1945-56.

Committee on Educators - Discrimination in Higher Education, Chairman, Midwest Section, 1945-56.

Committee on Equality of Opportunity in Higher Education, American Council of Education, 1950-

LaRabida Sanitarium, Board of Directors, 1946-48; Research Consultant, 1934-

Research Committee, Hertzler Research Foundation, 1948-

Affidavit

National Foundation for Infantile Paralysis, Inc.-Illinois Chapter General Medical Advisory Committee. Respirator Treatment Center Subcommittee, 1948-50.

Pan-American Board of Education, 1949-51.

National Paraplegia Foundation - Medical Advisory Committee, 1947-

Consultant in Physical Medicine and Rehabilitation - Veterans Administration, 1947-52.

Mayor's School Board Nominating Committee, 1947-53.

Y.M.C.A. of Chicago, Board of Managers, 1955-59.

Pan-American Institute of Educational Relations, 1948-

Hektoen Institute for Medical Research, Board of Trustees, 1945-

President, National Commission for the Prevention of Alcoholism.

President, International Commission for the Prevention of Alconolism.

Advisory Board Provident Hospital, 1947-50.

Consultant and Referee, National Science Foundation, Washington, D.C., 1959 to present.

H E W Release of September 7, 1963

Office of the Secretary
Washington 25, D. C.

FOR RELEASE AT CONCLUSION OF NEWS CONFERENCE
Saturday, September 7, 1963

RESULTS OF ANALYSIS OF "KREBIOZEN"

The Food and Drug Administration has identified the "Krebiozen" powder given to its inspector by Dr. Stevan Durovic and Dr. Andrew C. Ivy on July 12, 1963, as creatine. Creatine is an amino acid derivative plentifully available from meat in the ordinary diet and is a normal constituent of the human body. It is readily available as an inexpensive laboratory chemical.

The identification of "Krebiozen" resulted from the analysis of the powder by several scientific methods. This was undertaken under the supervision of Dr. Frank H. Wiley, Director of FDA's Division of Pharmaceutical Chemistry.

The first step was the re-examination of the infra-red spectrogram supplied by Dr. Durovic to the National Cancer Institute in September1961 and the infra-red spectrograms made by the National Cancer Institute from the small samples (1.5 mg. of powder and 5 mg. of crystalline material) supplied to it at the same time. These curves were all quite similar. On the basis of these tracings, the Division's Spectrophotometric Unit, under the direction of Mrs. Alma Hayden, attempted to identify the material from which the tracings were

made. They duplicated the curve submitted by Dr. Durovic by using a sample of creatine hydrate. The curve obtained by the National Cancer Institute on the powdered material was that of creatine which had absorbed a small amount of moisture.

The second step was to do a considerable amount of work on creatine obtained in pure form from chemical supply houses. This creatine was examined by infra-red spectrophotometry, by x-ray diffraction to study its crystal structure, by microscopic study of the crystals, and by mass spectrographic methods, preliminary to opening the vial containing the material supplied by Dr. Durovic and Dr. Ivy on July 12, 1963, and described as "Krebiozen."

The third step was the examination and identification of the contents of that vial. To supplement the evidence to be obtained by infra-red methods, the Food and Drug Administration enlisted the aid of other of its scientists and experts from other Federal agencies and from universities:

Microscopic Crystallography

William Eisenberg and Arnold Schultze, Division of Microbiology, FDA

Dr. Raymond Castle, University of New Mexico

X-ray Crystallography

Miss Mary Mrose of the Geological Survey, Department of Interior

Dr. William Bradley, University of Texas

Mass Spectrographic Studies
Joseph Damico, Division of Food, FDA

Dr. Klaus Biemann, Massachusetts Institute of Technology

In addition, the Food and Drug Administration asked Dr. Ellis R. Lippincott of the University of Maryland to work on the infra-red studies. Representatives of the National Cancer Institute and the Division of Biologics Standards of NIH, the Geological Survey, and the National Bureau of Standards also assisted the FDA's Bureau of Biological and Physical Sciences.

The small sample (approximately 2 mg.) was weighed and divided. An infrared spectral curve was made. This "fingerprinted" the material Dr. Durovic had supplied. It was creatine. This was then converted to creatinine, to which creatine changes when treated with hydrochloric acid. The converted product was identified by spectral curve as creatinine. Only creatine could have produced the creatinine by the treatment used. X-ray diffraction studies next confirmed the creatine identity. Crystallographic studies established that the powder was creatine. Mass spectrographic studies, conducted at Massachusetts Institute of Technology, established that the material was either creatine or creatinine. All of these tests leave no doubt as to the identity of the powder Dr. Durovic labeled "Krebiozen."

Creatine is in muscle tissue, and in blood in lesser amounts. The human body will produce in 24 hours as much as 100,000 times the amount of creatine as the alleged content of "Krebiozen" in one ampule. The

chemical was tested some time ago against animal tumors in the routine cancer chemotherapy screening program of the National Cancer Institute. It was found to be ineffective even in very high doses.

Laboratory studies are continuing to determine how much, if any, of this substance can be dissolved in mineral oil and how much, if any, is in the ampules of "Krebiozen" which FDA has obtained.

FDA is continuing its investigations of all of the facts regarding "Krebiozen."

H E W Release of October 16, 1963

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
Office of the Secretary
Washington 25, D. C.

FOR RELEASE IN A.M. PAPERS
Wednesday, October 16, 1963

The Department of Health, Education, and Welfare today released a report from the Director of the National Cancer Institute concerning his decision not to undertake clinical testing of Krebiozen.

The statement was accompanied by a report from the committee of cancer experts which reviewed the records of 504 patients treated with Krebiozen. The committee unanimously recommended against clinical testing of Krebiozen.

TO: The Secretary

THROUGH: The Surgeon General and
The Director, National Institutes of Health

FROM: The Director, National Cancer Institute

SUBJECT: Clinical Trial of "Krebiozen" Under National Cancer Institute Sponsorship

In mid-August of this year, I appointed a committee to review clinical records on patients treated with "Krebiozen"

and to recommend whether or not the National Cancer Institute should sponsor a clinical trial of "Krebiozen." The committee has been engaged in an extensive study of clinical records, microscopic slides, X-rays, and other records of these patients and has now completed its study and submitted a report to me. A copy of the report is attached.

The committee is unanimous in its conclusion that "Krebiozen" is ineffective as an anticancer drug and strongly recommends that no clinical trial be undertaken.

On the basis of this report, the findings of the Food and Drug Administration that "Krebiozen" is creatine and my own study of the extensive data previously submitted by Doctors Ivy and Durovic, I concur in the committee's findings and have determined that the National Cancer Institute will not sponsor or participate in a clinical trial of "Krebiozen."

As with any other potentially experimental drug, clinical trial of "Krebiozen" would have to be justified on one of three grounds. "Krebiozen.' does not qualify on any one of the three.

The first basis upon which a drug might be considered for clinical trial is theoretical. The proponents of "Krebiozen" have advanced the theory that "Krebiozen" is a tissue hormone which inhibits the multiplication of cancer cells. The Food and Drug Administration had demonstrated that "Krebiozen" is not a tissue hormone but rather creatine, a normal component of the human body concerned primarily with muscle contraction.

The second basis for a clinical trial, and the one upon which most are based, is that the drug must possess consistently strong anticancer activity in experimental animals. "Krebiozen" does not qualify on these grounds.

The third basis is the accidental discovery that a drug has anticancer activity in human beings. If "Krebiozen" had been shown to possess such activity despite the failure to satisfy the other two justifications for trial, I would have been prepared to sponsor a controlled clinical trial after appropriate animal toxicity study and the development of a procedure for the control of the identity of the substance.

HEW Release of October 16, 1963

The committee's report of the 504 case records clearly establishes that "Krebiozen" does not possess any anticancer activity in man.

The National Cancer Institute has completed its consideration of "Krebiozen." There is no justification for a clinical trial, and from a scientific standpoint we regard the case closed.

H E W Release of January 30, 1966

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
Food and Drug Administration
Washington, D.C. 20204

Sunday, January 30, 1966

Statement on the Krebiozen Case Following
Acquittal of Dr. Andrew C. Ivy,
Marko Durovic and Dr. William F.P. Phillips

A vast effort has gone into the trial of this tremendous case. Now the jury has concluded that the Government has failed to prove beyond a reasonable doubt that Andrew C. Ivy, Marko Durovic and William F.P. Phillips were responsible for causing the distribution of Krebiozen with the intent of defrauding the public.

Scientifically, however, this case was closed in 1963. FDA inspectors discovered in that year that Krebiozen had not been made as its promoters claimed. Later, following the procedure described by Steven Durovic for the production of Krebiozen from horse's blood, FDA scientists learned that the procedure did not work and that no so-called Krebiozen powder could be produced is the way Durovic claimed it had been produced.

FDA scientists, with the help of university and other outside consultants, analyzed a sample furnished by Steven Durovic and Dr. Ivy as pure Krebiozen and found it to be a common laboratory chemical, creatine. These chemists analyzed Krebiozen ampules, ready for injection into patients, and found them to contain only

mineral oil, sometimes with a small amount of a creatine derivative and an alcohol.

Also in 1963, a group of 24 of this Nation's best cancer experts, assembled by the National Cancer Institute, studied the medical records of 504 selected patients on whom the drug was supposed to have been effective, and found that there was no satisfactory medical evidence to support the idea that Krebiozen had had any anti-cancer effect whatever.

The Government has said since 1961 that it was prepared to make a test of Krebiozen if presented with any scientific data that would justify such a test. In collecting the data to determine whether a test was justified FDA found that there was no such thing as Krebiozen as an anti-cancer agent and that the promoters of the drug had been victimizind cancer patients into buying ampules of mineral oil.

Under the law there can be no commercial distribution of any new drug in the United States unless it has been approved as "safe" and "effective." Krebiozen has never been approved, and it does not now meet the standards for distribution even for investigational use.

Cancer victims and their families should be warned not to risk their lives or to throw their money away on this worthless drug. Evidence presented at the trial established that some patients accepted Krebiozen as a treatment, instead of X-ray or surgery, and thus allowed their disease to progress beyond control. Cancer can be cured in many cases by prompt medical attention. Delay means almost certain death.

H E W Release of January 31, 1966

U.S. DEPARTMENT OF
HEALTH' EDUCATION' AND WELFARE
Food and Drug Administration
Washington, D.C. 20204

Monday, January 31, 1966

Statement Following Acquittal of Dr. Stevan Durovic and The Krebiozen Research Foundation

The decision in Chicago was a disappointment to the Food and Drug Administration. However, it does not alter the determination of the Commissioner of Food and Drugs and the Agency to keep Krebiozen out of interstate commerce as a so-called anti-cancer agent. As far back as 1963 Krebiozen was proved to be nothing more than mineral oil and creatine, a common laboratory chemical. That scientific judgment still stands.

The FDA will carry out its responsibility to the public by doing whatever will be necessary to keep Krebiozen out of interstate commerce. We will do this as a life-saving activity. Each day a person with treatable cancer relies upon Krebiozen is a day that brings him closer to death.

HEW Release of March 31, 1966

U.S. DEPARTMENT OF
HEALTH' EDUCATION' AND WELFARE
Food and Drug Administration
Washington, D.C. 20204

March 31, 1966

STATEMENT BY COMMISSIONER GODDARD

As a physician, I am deeply concerned about the treatment and cure of cancer. The finest medical talent in the world is engaged in research for drugs to fight cancer. I know that there are several hundred people who believe in their hearts that Krebiozen will cure them. And I have deep sympathy for those people. But there are 198 million people whose health and safety depend in some measure on the integrity of FDA. For the sake of those 198 million people we must be forthright. We must adhere to the findings of science.

Medical science rendered its verdict in 1963. It proved that Krebiozen is nothing but mineral oil to which is occasionally added a common laboratory chemical called creatine and is worthless as an anticancer agent.

The sponsors of Krebiozen have never fulfilled the requirements of the laws passed by the Congress for the introduction of safe and effective drugs to the American public. They have held out false hope to unknown numbers of cancer victims. I am sympathetic with those who have been victimized by the Krebiozen hoax. I urge them and all patients with treatable cancer to seek professional medical help.

HEW Release of March 31, 1966

The Commissioner of Food and Drugs has neither the moral nor the legal right to disregard the laws of Congress and the evidence of science. We cannot and will not permit the jurisdiction of Krebiozen into interstate commerce.

James L. Goddard, M.D.
Commissioner of Food
and Drugs

Affidavit of Marco Durovic in Support of Petition of Certiorari

State of New York :
County of New York : ss.:

Krebiozen was brought to this country in 1949 by Dr. Stevan Durovic, a Yugoslavian physician and researcher, who emmigrated to Argentina in 1942, after his country was occupied by Nazi Germany.

The product was tested at University of Buenos Aires, Veterinary School, first by the then Dean, Dr. Ernesto Canepa, and after his death by Professor Dr. Anibal Da Grana.

In 1949, Dr. Durovic contacted Dr. A.C. Ivy and presented to him the protocol and results of experimental data. Dr. A.C. Ivy, a world known physiologist, was then Vice President of the University of Illinois, the Head of Department of Clinical Science, the Executive Director of the National Advisory Cancer Council and the Director of the American Cancer Society. Dr. Ivy showed deep interest in the results obtained and the scientific basis of the theory of the drug and immediately formed a group of physicians, which he headed, for further study and experimentation of the drug.

After the preliminary study on rats and dogs showing that the substance was not toxic in 10-100 times proposed human dosage, the experimenters started on the human patients in the fall of 1949. In the following eighteen months, twenty-two patients were treated. The results of this first experimental work with the scientific basis of the theory were published in a brochure, which was distributed to scientists and professionals in a meeting of March 26, 1951. This

meeting was called by Dr. Ivy aimed to enlarge experimentation of the product. The drug was offered and given without charge to physicians and to scientific and medical centers who were interested and willing to test it.

The Krebiozen Research Foundation was formed about that date. The Foundation had no means to finance the experimental work and only offered the drug without charge.

Shortly after the March, 1951 announcement, some big pharmaceutical houses approached us with very attractive offers to obtain the rights of production and expolitation of the drug, which we at this time did not accept, despite the encouraging results, because the drug stili was in the experimental stage.

In May 1951, the Treasurer of American Medical Association, Dr. J.J. Moore visited Dr. Stevan Durovic and Mr. Marko Durovic in the offices of Krebiozen Research Foundation. He insisted that the economic exploitation of the drug be given to a group of businessmen which had before shown interest in Krebiozen. He took a threatening position and provoked an argument with Marko Durovic, who protested against the interference and pressure being exerted by Dr. Moore on behalf of the A.M.A. in regard to the commercialization of Krebiozen. These facts are a part of the extensive sworn testimony given before the Joint Committee of the Illinois General Assembly by interpretor Dr. Peter Neskow in 1953-1954. Dr. Neskow was the interpretor for the Durovics during the meetings with J.J. Moore.

Affidavit

The pressure on the Durovics to make a deal with the Chicago businessmen continued through June, July and August of 1951. Dr. Ivy was requested by Dr. Moore and others associated with the A.M.A. to use his influence on the Durovics. This he refused to do, stating that his interest in the drug was purely scientific.

When this failed, a statement appeared in a Chicago newspaper to the effect that the American Medical Association was preparing a critical study of Krebiozen.

At once Dr. Durovic, in the name of Krebiozen Research Foundation wrote a letter to Dr. George Lull, the Secretary of the American Medical Association, in which he stated that it would be premature to issue any conclusive report on the effect of Krebiozen at such an early date, but that the Krebiozen Research Foundation was willing to cooperate in every way possible with the American Medical Association and was putting at its disposal all the research data gathered by the Foundation to that date.

At the same time, photostatic copies of clinical histories of one hundred and forty cancer patients who had been treated with Krebiozen were sent to the American Medical Association. These clinical histories detailed very favorable results obtained with Krebiozen on the one hundred and forty patients.

It was at this time Dr. Ivy received a "friendly letter" from Dr. Franklin Bing, former Secretary of the Council on Food and Drugs of the American Medical Association, in which Dr. Ivy was warned to deny publicly that Krebiozen was of value. Otherwise, he and his family would be submitted to all the punishments set out in Dr. Bing's letter, including loss of his position,

and moral and scientific annihilation.

On October 27, 1951, the American Medical Association published, in the Journal of the AMA, a so-called Status Report on Krebiozen, denying the effect of the drug in the treatment of cancer patients and which concluded: "These findings fail to confirm the beneficial effects reported by Dr. Ivy and associates."

Not one of the one hundred and forty cases, of which photostatic copies of the clinical histories were sent by Dr. Durovic to the American Medical Association on September 3, 1951, was included in this report.

A commission of the Illinois General Assembly was formed at the University of Illinois to investigate the controversy of Krebiozen in the beginning of 1953. As a consequence of the AMA Report, the University's medical staff was divided. The then President George Soddard took an adverse position against Dr. Ivy and the experimentation of Krebiozen, even though this was a private experimentation and not connected with the University.

The Commission subpoened all the papers of the American Medical Association in connection with the Status Report on Krebiozen. From those papers it was established that the Status Report of AMA was not only premature, but dishonest and in a large part fabricated.

In regard to this 'Status Report' of the AMA, we wish to quote from a speech made on the Floor of the Senate on December 6, 1963, by the Honorable Paul H. Douglas, then Senator of Illinois (Ex. P. submitted with the answer to interrogatories, October 2, 1970):

Affidavit

"Let me say for the sake of the record that when the AMA issued its 'status report' on 100 proved cancer cases treated with Krebiozen, which has served ever since as the backbone of all opposition to this preparation, 73 of the 100 cases were so close to death when Krebiozen treatment was begun that 40 only received only 2 injections, and the other 33 received only 4 injections of Krebiozen.

The report of the AMA also omitted all mention of objective cancer regression recorded in the medical records of 18 of these patients; and, on the basis of its survey, covering only a few weeks to a few months, the report characterized all of the 100 patients as dead or dying.

However, of the 23 remaining patients, 10 were alive and well, and appeared in person before the Illinois Legislative Commission on Krebiozen in 1954, and 7 of them are still alive and well today, in December, 1963, as follows:

Alive in 1954: Mrs. Julian Howard, Mrs. Cecile Luebkemann, Mrs. Catherine Firnsthal, Irene O. Kibby, A.M. Howard, Eleanor Gahan, Helen Arndt, Magda Johansen, Evelyn Vogel, and Irene P. Pietrowicz.

Alive in December 1963: Mrs. Julian Howard, 2429 West Berenice Street, Chicago; Mrs. Cecile Luebkemann, 6439 Newgard Street, Chicago; Irene O. Kibby, 2021 West 73rd Court, Elmwood Park, Ill.; A.M. Howard, 9410 North Monticello Street, Skokie, Ill.; Eleanor Gahan,

1619 Garfield Boulevard, Chicago; and Madga Johansen, 3810 North Troy Street, Chicago, now in Norway, who, I understand, is willing to fly here to testify. Evelyn Vogel, 1820 West Nelson Street, Chicago.

These are people who the AMA in 1951 said were either dead or dying."

The motive for such an action by the AMA is thoroughly exposed in Exhs. D and F submitted October 2, 1970, and also by reference to Exh. P, supra, the speech of former Senator of Illinois, the Honorable Paul H. Douglas:

"As to the AMA, I do not make the statements; we merely reproduce statements made by no less than five persons. The then treasurer of the American Medical Association is alleged to have said that unless control over Krebiozen were given to two gentlemen, one with the same name as the AMA treasurer, but not apparently related, he would see to it that the AMA destroyed the reputation of Krebiozen. This statement may not be true. But it was corroborated under oath by five persons before an Illinois legislative committee.

I spoke yesterday with a member of that Commission and asked him if he remembered that testimony. He said he did. Furthermore, he said that the testimony was given under oath."

It can be stated that the "Status Report" of the AMA, which was published in the J.A.M.A. in October, 1951, is the only opinion, and the only evaluation of Krebiozen which is formally accepted by organized

medicine and those who control cancer research in U.S. Government Agencies.

Since then, the evidence will show that the American Medical Association tried to discredit Krebiozen scientifically, and to impede an honest evaluation of the drug by an unprejudiced clinical trial.

In a sincere effort to end the unfortunate and unnecessary controversy of the value of Krebiozen, Drs. Andrew C. Ivy and Stevan Durovic proposed to the American Medical Association, first in 1951, then in 1953, and again in 1954, that a clinical test on patients be undertaken to determine whether Krebiozen had any biological effect on terminal cancer patients. In all of those occasions the AMA refused such test or any other.

In February 1958, the Krebiozen Research Foundation submitted a proposal for testing Krebiozen to the American Cancer Society. The ACS stalled the proposal for many months and finally rejected it.

In relation to the later development of cancer research and the subsequent position of Krebiozen, the letter written by Dr. Ivy in July, 1958 to Dr. Harold Diehl, M.D., Senior Vice President for research of American Cancer Society is of special scientific interest. In this letter, urging the test of Krebiozen, by ACS, Dr. Ivy wrote:

> "Dr. Durovic theorized that "Krebiozen is present especially in the reticulo-endothelial (RE) cells, which as is well known, react to various stimuli. When these cells are appropriately stimulated, Krebiozen, which is not present in the blood (except in traces

perhaps) under normal conditions, is released and can be extracted from the blood plasma" (1, 2). To stimulate the RE cells, he chose an extract of Actinomyces bovis, a mold which causes a tumor consisting in part of RE cells. He theorized that since this organism stimulates RE cells to multiply, it should cause RE cells to increase their secretion of an anti-tumor or anti-cancer factor into the bloodstream from which it could be extracted. He used an organic or a fat solvent, like benzene or ether, which is logical because certain physiological active substances in RE cells are soluble in such fat solvents, as well as in water. After evaporating the organic solvent Krebiozen was extracted by water from the fatty residue.

In our monograph published in 1956, it was stated: 'Since the start of this (the Krebiozen) investigation, and especially since 1951, we have been gratified to note the growing interest in the problem of the mechanisms concerned in providing the body with a natural resistance to cancer and how this resistance may be increased . . . ..'

It is gratifying to read in the Sloan-Kettering report the statement that 'There is reason now to believe that natural defenses against cancer exist. It has proved possible by manipulating and enhancing these defenses, to cure laboratory animals with some types of transplanted cancer.'

Affidavit

It is further stated in the Sloan-Kettering report, that 'different kinds of cancer may stimulate a common cancer resistance factor, or that different kinds of cancer have something in common that stimulate bodily resistance.' This agrees with our observations that Krebiozen is of value in the treatment of some patients who have different types of cancer.

More pertinent to the Krebiozen theory and our therapeutic observations are the statements in the Sloan-Kettering report 'that Zymosan does not inhibit the cancer directly but acts in some way in mice to enhance their natural defenses, tipping the scales in favor of the endangered host and against the cancer,' and 'Zymosan, unfortunately, is too toxic in man for clinical use.' Zymosan represents a substance extracted from yeast. Actinomyces bovis is a mold, a relative of the yeasts. When an extract of Actinomyces bovis is injected into mice with tumors, some tumors liquefy and slough out. But the extract of Actinomyces bovis, like Zymosan, is too toxic to use on man. But, Dr. Durovic, to avoid this toxicity, injects horses with the Actinomyces bovis extract, making the horses slightly ill, so that the RE cells secrete the resistance factor, 'Krebiozen', into the blood from which it is extracted, and finally made ready to be given to the cancer patient without making the patient sick. Theoretically, Zymosan, if injected into a horse, might also cause the secretion of Krebiozen into the blood." (footnotes omitted.)

III.

In August, 1958 Senator Paul H. Douglas of Illinois in a Senate speech proposed that the National Cancer Institute undertake substantially the same test the Krebiozen Research Foundation had submitted earlier to the American Cancer Society and remarked: "This is a fair test. It can do no harm. It might do great good."

The Krebiozen Research Foundation and Drs. A.C. Ivy and Stevan Durovic accepted this proposal at once. An exchange of lengthy letters with the National Cancer Institute followed for several years without any concrete results.

Finally, a meeting was held on October 20, 1960, between the Director of the National Cancer Institute, Dr. Kenneth Endicott, Dr. Sessoms of the NCI, Dr. A.C. Ivy and Dr. Durovic. At this meeting the parties agreed that a clinical test of Krebiozen could proceed when the Krebiozen Research Foundation and Drs. Ivy and Durovic had summarized all the clinical data gathered by the Foundation and had submitted them to the National Cancer Institute.

Accordingly, on September 29, 1961, Dr. A.C. Ivy, Dr. Stevan Durovic and Dr. John Pick met with Dr. Kenneth Endicott and Dr. Sessoms of NCI in their offices in Bethesda, Maryland and turned over to them an extensive study comprising of eight chapters covering clinical histories and observations on approximately 4200 patients, as well as extensive data concerning hypothesis, production, chemistry, toxicology, etc. (Ex. 4, of Oct. 2, 1970.)

Affidavit

In July 1962, Senator Douglas made another speech on the Floor of the Senate titled "National Cancer Institute Apparently Seeks to Delay or Avoid Clinical Test of Krebiozen." In his speech Senator Douglas stated:

> "We have tried for years to get the National Institutes of Health to institute such an objective test. They have consistenly and persistently refused. I believe they have refused in large part because at the beginning of this work Dr. Ivy got into a dispute with the American Medical Association, and the American Medical Association has refused to grant it any credence and on the contrary has attacked it bitterly."

and furthermore:

> "I believe that the National Institute of Health have become bureaucratic, because of the amount of money that has been poured into them, and have fallen under the control largely of the pundits of the American Medical Association and are ruled by the prejudices of organized medicine. The prejudices of medicine go far, Mr. President." (Congressional Record of the speech of Senator Paul H. Douglas of July 20, 1962.)

No clinical test was ever performed by the N.C.I. in spite of the agreement reached with its director Dr. Endicott in October, 1960.

Affidavit

Dr. Kenneth Endicott, director of the National Cancer Institute testified in the Krebiozen Criminal Trial (64 Cr. 668 U.S.D.C., N.D. Ill.). We quote:

> Q. Mr. Witness, it is a fact, is it not, that not a single biological test was ever made of the cancer substance Krebiozen? A. By me?
>
> Q. By the National Cancer Institute, sir? A. Yes, Sir, I think that is true.

Dr. Endicott also testified regarding clinical tests performed by the N.C.I. In answer to a question by Attorney Sembower concerning how many drugs were clinically tested each year, Dr. Endicott stated:

> Q. Approximately how many drugs were you testing each year? A. About 36,000, perhaps something like that per year. I cannot be exact, but it is in that general range.
>
> Q. How many of these involve animal experimentations? A. All of them.
>
> Q. How many, then, would involve human administration? A. Well, there is no constant ratio because you can never tell how many are going to look good, but perhaps 20 or 30 compounds or natural products out of 30-odd thousand would reach the stage of being tried in man in the course of a year, something on that order. It might range from as low as seven or eight up to 40, but it is in that general area. (64 CR 668, Transcrip. P. 6575, 6676)

Affidavit

* * * *

Instead of undertaking a test of the drug, the Department of H.E.W., on September 7, 1963, issued a press release that the Food and Drug Administration had identified the Krebiozen powder given to them by Dr. Stevan Durovic as creatine (64a).

About the same time, Dr. Endicott, the Director of the National Cancer Institute, appointed a Committee of Physicians, in which were many employees of the NCI, and also people who received grants from the Institute to evaluate Krebiozen. The Committee met secretly in a motel near Washington, D.C. to allegedly evaluate Krebiozen.

In October, 1963, another press release by the Department of HEW was issued with a statement by the Director of N.C.I. In this release the Director stated that Krebiozen is not a tissue hormone, but creatine, that the drug does not possess any anti-cancer activity in man, that the National Cancer Institute has completed its consideration of Krebiozen and that there is no justification for a clinical trial (68a).

On October 28, 1964, Dr. Stevan Durovic and Marko Durovic were indicted, by a suppressed indictment, and charged with violating the Food, Drug and Cosmetic Act. This indictment was extended on November 17, 1964, in a forty-nine count indictment. Besides Dr. Durovic, Marko Durovic, and the Krebiozen Research Foundation, Dr. A.C. Ivy and Dr. William Phillips were included (64 CR 668).

Affidavit

At the end of January, 1966, after more than nine months of trial, all the defendants were acquitted on all charges.

Immediately after the verdict of the jury in The Krebiozen trial, the F.D.A. issued a press release stating that for them: "Scientifically, this case was closed in 1963". The F.D.A. simply ignored the fact that in the nine months of trial it had been established that they had used false spectra and false analysis in evidence (72a).

IV

It is paradoxical to view the stands of the official Health Agencies which on one side are discrediting and destroying the results of Krebiozen, and, on the other side, are presenting the theory of Krebiozen as an important advancement in the field of cancer. This is especially true in light of the fact that Krebiozen is in a far advanced stage as a product, and is non-toxic, as compared with others.

On September 21, 1972, the National Cancer Institute of the United States Department of Health issued a press release, stating:

> "An international conference on the use of BCG in treating cancer will be held October 5-6 at the National Cancer Institute, one of HEW.s National Institutes of Health, Bethesda, Maryland.
>
> Scientists think that BCG works by stimulating the patient's immune system mobilizing the body's defensive cells, such as, lymphocytes and phagocytes, for. scavenger cells, which then

attack the cancer cells. It is hoped that the results of experiments on animals, which are aimed at a better understanding of how BCG acts will shed light on how to make its use in human therapy more reliable."

Despite the fact that their reported results were termed "variable", the meeting of October 5 and 6, 1972, was viewed as a milestone marking progress in what is now known as the immunology of cancer, and is today considered a major development in cancer research.

As was noted at the meeting, this is not a new approach to the problem of cancer, but goes back "at least 13 years" to the time when workers at the Sloan-Kettering Institute found, first that Zymosan (a toxic yeast), and then that BCG (a live but attenuated TB bacillus), could rouse the immune system of animals to fight cancer.

This is the orthodox version. It ignores the fact that the pedigree for the BCG work dates back even further, to the disputed cancer drug Krebiozen, which was introduced to the scientific world more than 20 years ago by Dr. Stevan Durovic.

Dr. Durovic was the first to maintain that the body possesses its own natural defense against cancer. He was the first to declare that this defense resides in the reticuloendothelial system, that cancer results from insufficiency of this system, the one to protect and repair the body through the production of lymphocytes, antibodies and the like. He was also first to demonstrate that through appropriate stimulation this system could be induced to produce more than normal amounts of the anti-cancer factor.

Affidavit

This is exposed in many publications discussing the question of Krebiozen and especially in the patent applications filed by Dr. Durovic in 1951 and 1958, which reads:

> "Any appropriately made extract of any living organism which causes a proliferation of the reticuloendothelial cells, or causes a granuloma or a cancerous growth will also, when injected into an animal cause the production in the animal of a growth regulating substance. . . . In carrying out my method of producing a drug or substance having the characteristics referred to above, it is necessary to select an agent which is known objectively to stimulate the reticuloendothelial system. I have elected, as an example of such an agent, Actinomyces bovis, which is a fungus-like mico-organism causing in cattle a marked granulomatous reaction and tumor formation. . . ." (Emphasis added.)

Between these statements, and the NCI's recently released position paper on BCG, there is only a sematic difference.

The NCI states:

> "Among the major developments in cancer research in the past two decades has been the demonstration that the immune system of animals can be stimulated in such a way as to make the animals more resistant to cancer or under very special circumstances, to cause the destruction of already established tumors."

Sloan-Kettering ventured to use Dr. Durovic's own designation of the "immune system" when it said in a recent release that "injections of BCG into animals increased the activity of the reticuloendothelial system."

The real difference between Dr. Durovic's work and that now underway is that he carried it a giant step further--a step which still awaits duplication by other cancer researchers.

Actinomyces bovis, like Zymosan, is too toxic for use in human patients. Thus, Dr. Durovic used his material to stimulate horses to produce an anti-cancer substance, extracted this substance from their blood, called it Krebiozen and used it to augment the depleted reserves of the cancer patient in a kind of replacement therapy.

Current workers with BCG use it directly on the cancer patient in an effort to stir up his own defective or damaged reticuloendothelial system to produce enought of the anti-cancer factor to cure his cancer.

The NCI stated: "Results have been variable, but in a few trails BCG when combined with other treatment has produced some encouraging but not definitive results" over the past eight years.

For instance, in a recent report of worker's at Sloan-Kettering, it was said that of sixteen patients with melanoma treated with BCG, one obtained "complete regression of skin lesions with no recurrence after 16 months with no further treatment."

Another participant at the meeting, Dr. Edmund Klein, reported "varying degrees of regression including microscopically proved eradication of malignant lesions" observed in some patients treated with BCG at Roswell Park Memorial Institute.

However, he noted that the response seemed to depend on the state of the patient's immunization system, that is, whether his reticuloendothelial cells were still able to respond to stimulation.

This doubtless accounts for the variability and inconsistency of the results reported for BCG, in contrast to those documented by Dr. Ivy and others for Krebiozen.

In being tested and researched for more than twenty years, Krebiozen has been subject of what is probably the most extensive investigation ever known in cancer research. In all, it involved 4,277 patients with thirty-five different types of cancer, treated by about 3,000 physicians. Of these patients, 97% percent were in the terminal stages of cancer when Krebiozen treatment was started, with a life expectancy from two days to six months, as estimated by their personal physicians.

In his 820-page analysis of these cases, presented to the NCI in 1961, Dr. Ivy claimed an unprecedented effectiveness for the drug; arrest, shrinking or disappearance of tumor in 86 percent of all cases (Exh. 4 October 2, 1970).

Of these once-terminal cancer patients, 114 had survived four to eleven years, Dr. Ivy said. Most of these are still alive and without evidence of cancer today.

The most telling aspect of the report, perhaps, was Dr. Ivy's resume of fourteen "twice opened" cases, patients who, prior to Krebiozen therapy, had undergone what is called "exploratory laparotomy". That is, they had been opened in the hope that their cancers could be removed surgically and promptly closed again, because their tumors were too widespread to allow operation. Several years later, after no other treatment than Krebiozen, a second laparotomy was performed for other purposes.

At the second operation no trace of cancer could be found in any of these patients.

Over the years, while Dr. Ivy, Dr. Durovic, and Krebiozen continued to be targets for orthodox condemnation, a spate of reports appeared in medical journals of experiments designed in one way or another to prove Dr. Durovic's theory--of course without mentioning his name. The Sloan-Kettering work mentioned above was one of them. As a result of such the public strictures and attempts to exploit their work without giving them credit, Drs. Ivy and Durovic became convinced that because of such prejudice, no favorable evidence of Krebiozen's activity --however convincing--would be accepted. Thus, they pressed time after time for a definitive clinical test, and time after time were refused.

Meanwhile, other men, who accept the insights discovered by Dr. Durovic, but at the same time deny their indebtedness, "slowly and laboriously" are attempting to have to repeat his work in disguished form.

However, they failed, as of the present, to reach the same results.

s/ Marko Durovic
MARKO DUROVIC

Sworn to and subscribed to me
this 17th day of July, 1973.

s/ Jerold W. Dorfman
NOTARY PUBLIC

JEROLD W. DORFMAN
Notary Public, State of New York
No. 31-6078665
Qualified in New York County
Commission Expires March 30, 1974

Proposed Joint Resolution of the 88th Congress

88thCONGRESS
1st SESSION

S.J.RES. 101

JOINT RESOLUTION

Authorizing and directing the National Institutes of Health to undertake a fair, impartial, and controlled test of Krebiozen; and directing the Food and Drug Administration to withhold action on any new drug application before it on Krebiozen until the completion of such test; and authorizing to be appropriated to the Department of Health, Education, and Welfare the sum of $250,000.

BY MR. DOUGLAS, MR. KEFAUVER, MR. BAYH, MR. CASE, MR. JAVITs, MR. KEATING, MR. PELL, MR. PROXMIRE, MR. SCOTT, and MR. WILLIAMS OF NEW JERSEY

JULY 18, 1963

Read twice and referred to the Committee on Labor and Public Welfare

S.J. RES. 101

IN THE SENATE OF THE UNITED STATES

July 18, 1963

Mr. Douglas (for himself, Mr. Kefauver, Mr. Bayh, Mr. Case, Mr. Javits, Mr. Keating, Mr. Pell, Mr. Proxmire, Mr. Scott, and Mr. Williams of New Jersey) introduced the following joint resolution; which was read twice and referred to the Committee on Labor and Public Welfare.

Proposed Joint Resolution

JOINT RESOLUTION

Authorizing and directing the National Institute of Health to undertake a fair, impartial, and controlled test of Krebiozen; and directing the Food and Drug Administration to withhold action on any new drug application before it on Krebiozen until the completion of such test; and authorizing to be appropriated to the Department of Health, Education, and Welfare the sum of $250,000.

Whereas hundreds of cancer patients now being treated with the drug Krebiozen believe their lives depend upon the continued use of the drug; and

Whereas Doctor Andrew C. Ivy, chief sponsor of the drug Krebiozen, and former head of the University of Illinois Medical Schools, is widely known for his work in cancer research as a former director of the American Cancer Society, as the contributor of a dozen or more papers on cancer research to leading medical journals, and as one of the foremost pathologists and medical and cancer research experts in the country today; and

Whereas The National Cancer Institute has investigated and tested thousands of substances for the control of cancer; and

Whereas many of these substances, unlike Krebiozen,

have had extreme toxic effects, such as 5-Fluorouracil (5-FU) and 5-Fluorodeoxyuridine (5-FUDR); and

Whereas the nontoxicity of the drug Krebiozen has not been disputed, and such drug has been used on over four thousand human subjects for periods of up to twelve years, and reports as to its effects have been submitted by about three thousand physicians; and

Whereas the clinical evidence submitted, with respect to the drug Krebiozen, by Doctor Andrew C. Ivy to the National Cancer Institute indicates that in varying kinds of tumors there has been an actual regression of the tumors in some cases, and relief of pain in many of these cases and in many others; and

Whereas the foregoing facts more than justify a fair test and a determination of the efficacy of the drug Krebiozen: Therefore be it

Resolved by the Senate and House of Representatives of the United States of America in Congress assembled, That the National Institutes of Health be authorized and directed to undertake immediately a fair, impartial, and controlled test, under the direction of competent clinical investigators, of the safety and efficacy of Krebiozen and to make to the Congress quarterly reports on the progress of such a test; and that the Food and Drug Administration withhold action on any new drug application before it on Krebiozen until the

complication of such test, and that for the purpose of conducting the test there is hereby authorized to be appropriated to the Department of Health, Education, and Welfare the sum of $250,000.

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6 *Moore's Federal Practice* (2d ed. 1948) — 14
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2 *Wigmore on Evidence*, § 561 (3d ed. 1940) — 14

In the Supreme Court of the United States

OCTOBER TERM, 1973

No. 73-168

MARKO DUROVIC, ET AL., PETITIONERS

v.

CASPAR W. WEINBERGER, ET AL.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SEVENTH CIRCUIT

BRIEF FOR THE RESPONDENTS IN OPPOSITION

OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-19a) is reported at 479 F. 2d 242. The findings of fact and conclusions of law of the district court (Pet. App. 22a-25a) are reported at 327 F. Supp. 386.

JURISDICTION

The judgment of the court of appeals was entered on April 25, 1973. The petition for a writ of certiorari was filed on July 23, 1973. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

QUESTIONS PRESENTED

1. Whether Krebiozen is a "new drug" within the meaning of the Federal Food, Drug, and Cosmetic Act because it has not been generally recognized by qualified experts as safe or effective for the treatment of cancer.

2. Whether Krebiozen, which has never been the subject of an effective new drug application under the Federal Food, Drug, and Cosmetic Act, is exempt from the effectiveness requirements added to the Act in 1962.

3. Whether the record in this case presented genuine issues as to material facts which precluded disposition of the case on cross-motions for summary judgment.

STATUTORY PROVISIONS INVOLVED

1. Section 505 of the Federal Food, Drug, and Cosmetic Act, 52 Stat. 1052, as amended, 21 U.S.C. 355, provides in pertinent part:

> (a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug.
>
> (b) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (1) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (2) a full list of the articles used as components of such drug; (3) a full statement of the composition of such drug; (4) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing

of such drug; (5) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (6) specimens of the labeling proposed to be used for such drug.

* * * * *

2. Prior to the Drug Amendments of 1962, Section 201(p) of the Federal Food, Drug, and Cosmetic Act, 52 Stat. 1041, 21 U.S.C. (1958 ed.) 321(p), provided in pertinent part:

> The term "new drug" means—
>
> (1) Any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this chapter it was subject to former sections 1–5 and 7–15 of this title, and if at such time its labeling contained the same representations concerning the conditions of its use; or
>
> (2) Any drug the composition of which is such that such drug, as a result of investigations to determine its safety for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

3. Section 201(p) of the Federal Food, Drug, and Cosmetic Act, as amended by the Drug Amendments of 1962, 76 Stat. 781, 21 U.S.C. 321(p), provides in pertinent part:

> The term "new drug" means—
>
> (1) Any drug * * * the composition of which is such that such drug is not generally recognized,

among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this chapter it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) Any drug * * * the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

4. Section 107(c)(4) of the Drug Amendments of 1962, 76 Stat. 789, set forth as a note following 21 U.S.C. 321, provides:

In the case of any drug which, on the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (C) was not covered by an effective application under section 505 of that Act, the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

STATEMENT

Petitioners manufacture, distribute, and promote Krebiozen, a drug prescribed for use as an agent in the management of malignant tumors (Pet. App. 2a). Since the introduction of Krebiozen in 1949, petitioners and others have sought unsuccessfully to obtain administrative [1] and judicial [2] approval to market the drug.

The Federal Food, Drug, and Cosmetic Act of 1938, as amended by the Drug Amendments of 1962, requires that an administratively approved "new drug application" ("NDA") be in effect before a "new drug" may be introduced in commerce. 21 U.S.C. 355. Under the statute, the Food and Drug Administration is directed to approve an NDA only where the drug is shown to be safe and effective for its intended use.

Prior to the 1962 amendments, Section 201(p) of the Act defined "new drug" as (1) a drug not generally recognized by qualified experts as safe for its intended use, or (2) a drug recognized as safe but which had not been used to a material extent or for a material time.

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[1] New drug applications, pursuant to 21 U.S.C. 355(b), were submitted to the Food and Drug Administration for Krebiozen by Marko Durovic on April 15, 1954, and by Stevan Durovic on March 27, 31, and April 13, 1961 (see Pet. App. 4a–5a).

[2] See *Rutherford* v. *American Medical Association*, 379 F. 2d 641 (C.A. 7), certiorari denied, 389 U.S. 1043; *Tutoki* v. *Celebrezze*, 375 F. 2d 105 (C.A. 7); *Ivy* v. *Katzenbach*, 351 F. 2d 32 (C.A. 7), certiorari denied, 382 U.S. 958; *Durovic* v. *Palmer*, 342 F. 2d 634 (C.A. 7), certiorari denied, 382 U.S. 820; and *United States* v. *Bukowski*, 435 F. 2d 1094 (C.A. 7), certiorari denied, 401 U.S. 911. Each of these cases is described in the opinion below (Pet. App. 8a–9a, n. 3).

The 1962 amendments added the requirement that the drug be generally recognized by qualified experts to be effective. The amendments also included a "grandfather" clause exempting from the new efficacy requirements any drug (in the generic sense [3]) which, on the day before the amendments became effective, was "(a) commercially used or sold in the United States, (b) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (c) was not covered by an effective [NDA] * * *" (Section 107(c)(4), 76 Stat. 789, set forth as a note following 21 U.S.C. 321).

In May 1968, an investigation by the Food and Drug Administration indicated that petitioners were distributing Krebiozen in interstate commerce, in violation of Section 505(a) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 355(a). On the basis of this information, the agency issued a notice of hearing to petitioners, pursuant to Section 305 of the Act, 21 U.S.C. 335, informing them that a criminal proceeding against them was being contemplated.

On January 7, 1969, petitioners instituted the present action for a declaratory judgment that the new drug applications for Krebiozen had become effective or, in the alternative, that Krebiozen was exempted from obtaining an approved NDA by Section 107(c)(4) of the Drug Amendments of 1962. The government answered that Krebiozen is and at all times has been a new drug for which there has never been an

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[3] See *USV Pharmaceutical Corp.* v. *Weinberger*, No. 72-666, decided June 18, 1973.

effective NDA. After discovery, both parties moved for summary judgment.

In support of its motion for summary judgment, the government submitted affidavits describing the administrative history of Krebiozen and the views of qualified experts as to its safety and effectiveness as an agent for controlling malignant tumors. The affidavit of Dr. Marion J. Finkel, Deputy Director of FDA's Bureau of Drugs, stated that the agency has never approved an NDA for Krebiozen and that applications submitted for the drug in 1954 and 1961 had been refused because they were incomplete and inadequate. Petitioners never sought judicial review of those refusals. Thus, as petitioners now concede (Pet. 19), neither before nor after the 1962 amendments has Krebiozen been the subject of an effective NDA.

The affidavits of Dr. Jesse L. Steinfeld, Surgeon General of the United States, and Dr. Carl G. Baker, Director of the Public Health Service's National Cancer Institute, both qualified experts in cancer research and chemotherapy, stated that Krebiozen has never been generally recognized as safe or effective for use in the treatment of cancer.

The affidavits stated further: (1) that no medical school teaches, or has taught, that Krebiozen is a cancer treatment; (2) that no hospital associated with a medical school uses Krebiozen to treat cancer; (3) that no expert in the field of cancer believes, or has ever believed, that Krebiozen is safe or effective for the treatment of cancer; (4) that the composition of Krebiozen was not known to any expert in the field of

cancer until an FDA analysis was conducted and the results released in 1963; (5) that the chemical substances identified by the FDA analysis—a creatine derivative, an alcohol, and mineral oil—are not recognized by cancer experts as having any therapeutic value in the treatment of cancer; and (6) that cancer experts, lacking information about Krebiozen's composition and biological activity, could not have formed an opinion prior to 1963 concerning the drug's safety.

Petitioners responded by submitting the affidavits of Dr. Andrew C. Ivy, a physician who has treated patients with Krebiozen, and Marko Durovic, who asserted neither medical nor scientific qualifications (Pet. 12a–13a). Dr. Ivy and Mr. Durovic stated their personal opinions that Krebiozen is a non-toxic and beneficial drug. Neither affidavit discussed whether Krebiozen was generally recognized by qualified experts as a safe or effective cancer treatment.

The district court granted summary judgment for the government, denied petitioners' motion, and dismissed the complaint (Pet. App. 20a–21a). The court found that the evidence submitted by petitioners did not controvert the affidavits of Drs. Steinfeld, Baker, and Finkel, and that those affidavits established that Krebiozen is not now and never has been generally recognized as safe or effective for the management or treatment of malignant tumors (Pet. App. 24a). On the basis of its findings, the court concluded (1) that no approved NDA is now or has ever been effective

for Krebiozen, (2) that Krebiozen is now and has always been a new drug, and (3) that Krebiozen is not protected by the grandfather clause of the Drug Amendments of 1962 (*ibid.*).

The court of appeals unanimously affirmed (Pet. App. 1a–19a). It held that, under the law prior to 1962, a drug product used for the treatment of a life-threatening disease such as cancer was not "safe," even though non-toxic, if it was ineffective. Under that definition, Krebiozen had never been generally recognized as safe (Pet. App. 15a–17a). The court reasoned further that, even if non-toxicity were the only test for safety, Krebiozen was a new drug prior to the 1962 amendments because at that time its identity and composition were so completely unknown that it could not have been generally recognized as safe by qualified experts (Pet. App. 17a).

ARGUMENT

Petitioners contend that they need not demonstrate to the Food and Drug Administration that Krebiozen is a safe and effective cancer drug. In their view, the drug ceased to be a "new drug" because it achieved general expert recognition as a safe treatment for cancer prior to the Drug Amendments of 1962 (and, by implication, still enjoys that status). Therefore, they claim, it is exempted from the amendments' efficacy requirements by the grandfather clause in Section 107(c)(4). They further claim that the district court should not have determined these questions on a

motion for summary judgment. These contentions turn on the particular history of Krebiozen as developed on this record. They involve no issue of general importance to the administration of the Federal Food, Drug, and Cosmetic Act and do not warrant review by this Court.

1. There is no support in this record for petitioners' claim that, since its introduction in 1949, Krebiozen has somehow ceased to be a "new drug."

First, Krebiozen has never met the test for general recognition of safety under the 1938 Act. Where a drug is to be used for the treatment of a life-threatening disease such as cancer, the concept of "safety" also comprehends effectiveness. This longstanding administrative construction was explained to Congress by the Secretary of Health, Education, and Welfare in 1961: "If the drug is offered for the treatment of progressive or life-threatening diseases, such as cancer, *or* if the drug is seriously toxic or has alarming side effects, we now consider its effectiveness."[4] The medical reasons for this interpretation were set forth in this record by Drs. Steinfeld and Baker in clear and simple terms: reliance on ineffective therapy, by delaying the institution of effective therapy, permits progression of a life-threatening disease beyond the point

[4] Hearings before the Subcommittee on Antitrust and Monopoly, Senate Committee on the Judiciary, on Drug Industry Antitrust Act, 87th Cong., 1st Sess., Part 5, p. 2588 (emphasis added).

where it can be controlled and increases the likelihood of death.[5]

When it was considering whether to add an effectiveness criterion to the Act, Congress was well aware that evaluations by FDA of the safety of therapeutic agents used in treating diseases like cancer necessarily included an evaluation of effectiveness as well. Indeed, the first Senate Report on the matter, which proposed conferring on FDA the power to suspend outstanding new drug applications for lack of effectiveness, made clear that this proposal was "in no way intended to affect any existing authority of the [FDA] to consider and evaluate the effectiveness of a new drug in the context of passing upon its safety."[6]

Petitioner urges that, if this standard is correct, there would have been no reason for Congress to make "effectiveness" an express statutory requirement. But this argument ignores the fact that the old standard, under which safety would be evaluated in conjunction with effectiveness, was limited to special categories

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[5] The affidavits said (Pet. App. 16a):

"The use of an ineffective drug such as Krebiozen for the treatment of a life-threatening disease such as cancer is not a safe medical practice. Any delay in the institution of effective therapy (*e.g.*, radiation, surgery, effective chemotherapy) caused by the use of an ineffective drug allows the disease to progress beyond control. Delay means almost certain death."

[6] S. Rep. No. 1744, 87th Cong., 2d Sess., Part I, p. 15. When the FDA's proposed authority to review drugs for effectiveness was subsequently broadened, Congress gave no indication of an intent to retreat from this position. *Id.* at Part II.

such as progressive, life-threatening diseases. There was thus a broad range of drugs, allegedly therapeutic for other conditions, which were first subjected to administrative scrutiny for effectiveness by the 1962 amendments.

Second, even apart from the weight to be accorded this administrative and congressional interpretation,[7] and assuming *arguendo* that "safe" means only "nontoxic," the record does not disclose expert general recognition of Krebiozen's safety. As the court of appeals correctly concluded, "[i]t is clear that neither Dr. Ivy's affidavit nor the reports and opinions of others, reported by Durovic's affidavit, purported to assert that Krebiozen had, as of October 9, 1962, achieved general recognition among experts as safe or safe and effective" (Pet. 15a).

It may well be that individual practitioners, such as Dr. Ivy, sincerely believe that the drug is safe and beneficial in the treatment of cancer (see Pet. App. 40a–41a). But the statute prior to 1962 required *general* recognition of safety by experts qualified to evaluate the safety of drugs, and still requires it today. Unless there is a consensus among the experts that a product is safe, it simply does not meet the standards of Section 201(p). See, *e.g.*, *United States* v. *An Article of Drug . . . "Bentex Ulcerine,"* 469 F. 2d 875 (C.A. 5), certiorari denied, No. 72–1198, June 11, 1973. The record in this case is devoid of evidence showing such a consensus. On the contrary, the affidavits of Drs. Steinfeld and Baker, both spe-

[7] Cf. *Udall* v. *Tallman*, 380 U.S. 1, 16–18.

cialists well acquainted with the relevant literature and the state of expert opinion concerning cancer research, declared without contradiction that no expert in the field of cancer believes or has ever believed that Krebiozen is safe or effective for the treatment of that disease. They also stated without contradiction that prior to 1963 experts in the field lacked information about the drug's composition and biological activity and therefore could not have entertained any opinion as to its safety.

2. Since Krebiozen has never been generally recognized by qualified experts as safe for use in treating malignant tumors, it is not entitled to exemption from the "effectiveness" requirements of the 1962 amendments under the grandfather clause in Section 107(c)(4). It fails to meet the second requirement of that clause—that the product not have been a new drug at the time the amendments became effective. Accordingly, Krebiozen is subject to the same standards that apply to other "new drugs," and petitioners must demonstrate by substantial evidence that the drug is safe and effective for its intended use before it may be distributed in commerce. 21 U.S.C. 355.

3. Petitioners' contention that the case should not have been decided on cross-motions for summary judgment is without merit. Their suit was a declaratory judgment action challenging FDA's determination that their product was a new drug for which an approved NDA should have been, but was not, in effect. Petitioners were afforded a full and fair opportunity to demonstrate that a genuine issue of material

fact existed which would preclude the entry of summary judgment under Rule 56, Fed. R. Civ. P. They offered only two affidavits in response to those submitted by the government's experts. Both courts below correctly found that neither affidavit contradicted the showing by those experts that Krebiozen had never achieved general expert recognition, either as safe or as safe and effective (Pet. 15a, 23a–24a).[8]

CONCLUSION

For the foregoing reasons the petition for a writ of certiorari should be denied.

Respectfully submitted.

ROBERT H. BORK,
Solicitor General.
THOMAS E. KAUPER,
Assistant Attorney General.
HOWARD E. SHAPIRO,
LEE I. WEINTRAUB,
Attorneys.

JEFFREY B. SPRINGER,
Attorney,
Food and Drug Division,
Department of Health, Education, and Welfare.

SEPTEMBER 1973.

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[8] Petitioners' contention, presented here for the first time, that they should be granted a trial in order to test the qualifications of experts whose affidavits were submitted on behalf of the government is without foundation. The issue of expert qualifications is ordinarily a matter for the reasonable discretion of the trial court. See, *e.g.*, 2 *Wigmore on Evidence*, § 561 (3d ed. 1940). Expert opinion in the form of affidavits may be used to support a motion for summary judgment. See 6 *Moore's Federal Practice*, pp. 2801, 2812–2813 (2d ed. 1948).

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No. 73-168

In the Supreme Court of the United States

OCTOBER TERM, 1973

MARKO DUROVIC, an individual and also known as MARKO DUROVIC, formally d/b/a DUGA LABORATORIES; STEVAN DUROVIC, d/b/a PROMAK LABORATORIES; and KREBIOZEN RESEARCH FOUNDATION, a corporation,

Petitioners,

VS.

CASPAR W. WEINBERGER, Secretary of Health, Education & Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food & Drugs,

Respondents.

PETITION FOR REHEARING OF ORDER DENYING PETITION FOR WRIT OF CERTIORARI

SOLOMON H. FRIEND
JEROLD W. DORFMAN
16 West 61st Street
New York, New York 10023
(212) 245-7052
Attorneys for Petitioners

Of Counsel:
ANNA R. LAVIN
EDWARD J. CALIHAN, JR.
53 West Jackson Blvd.
Chicago, Illinois 60604

UNITED STATES LAW PRINTING CO., CHICAGO, ILLINOIS 60618 (312) 525-6581

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Petitioners,

vs.

CASPAR W. WEINBERGER, Secretary of Health, Education & Welfare, and **ALEXANDER M. SCHMIDT**, Commissioner of Food & Drugs,

Respondents.

PETITION FOR REHEARING

Petitioners present their petition for a rehearing of this Court's order dated October 15, 1973, denying the petition for a Writ of Certiorari to the United States Court of Appeals for the Seventh Circuit, and, in support thereof, respectfully show:

GROUNDS FOR REHEARING

This Court, on October 15, 1973, denied petitioner's request for Certiorari, and let stand a decision granting the government's motion for summary judgment, and denying

petitioner's motion for summary judgment. The two issues raised by plaintiffs' complaint were, whether the drug Krebiozen was a "new drug" under the Food, Drug & Cosmetic Act, 21 U.S.C., Section 355, and whether a New Drug Application was presently effective for Krebiozen under that statute. An affirmative answer to either issue would have permitted the petitioner to market the drug in interstate commerce. In all of this time, however, petitioners presumed they would have the right to distribute the drug on a physician's recommendation in intrastate commerce; that is, within the State of Illinois.

However, on September 7, 1973, since the filing of petitioner's request for Writ of Certiorari, the Illinois legislature has amended the Illinois Food, Drug & Cosmetic Act to prohibit the selling or giving away of any "new drug" in Illinois, unless a New Drug Application has been approved under Section 505 of the Federal Act, exempting "any drug which is not a new drug as defined in the Federal Act." (See Illinois Public Act 75-599, Laws 1973, attached hereto.)

By refusing to grant petitioners a trial on the merits, this Court has not only prevented Krebiozen from moving in interstate commerce, but it has also, apparently, made distribution of the product illegal within Illinois *even where its use is recommended by a learned physician.*

The significance of this is that individuals who are present or past cancer patients, and who had been introduced to Krebiozen by their physicians can no longer continue to receive the drug in Illinois, in situations wherein the physician and patient believe the very life of the patient to be dependent upon a supply of the drug.

We have contended that the Seventh Circuit erred in not giving Plaintiff the opportunity to present evidence concerning general recognition of safety of the drug.

In the case of *Free* v. *Bland*, 369 U.S. 603, the Court decided that controverted allegations could only be resolved by trial on merits, not summary judgment.

We also urge that a grant of motion for summary judgment is often inappropriate where evidence bearing on crucial issues of fact is in the form of expert opinion testimony.

The Seventh Circuit stated:

> "We have been made aware, in this record of much of the emotionally charged controversy about Krebiozen. Some characterize Krebiozen as a hoax, yet there are many who believe with deep sincerity that a number of cancer sufferers have been aided, or even saved by it. Its advocates contend that the medical "establishment" both in and out of government has unfairly denied Krebiozen a reasonable test. So distinguished a person as the Honorable Paul Douglas, former Senator from Illinois has taken its part."

That Court by this admits the existence of genuine issues of material fact and the existence of controverted allegations, but denies the Plaintiff a day in Court and a hearing on genuine and substantial questions of fact.

In support of this question of fact we will mention only some of these opinions and reports which are contained in the record:

1.) Reports, clinical histories and opinion of 4,277 patients by about 3,000 licensed physicians, collated by Dr. A. C. Ivy. (Exhibit No. 4)

2.) Affidavit of Dr. A. C. Ivy of March 30, 1971 that the Krebiozen is safe and beneficial in the treatment of cancer.

3.) Affidavits of licensed physicians from April 1954 who used Krebiozen that the drug is safe in the management of cancer. (Exhibit No. 5)

4.) Affidavits of licensed physicians from March 1961 who used Krebiozen that the drug is safe in the management of cancer.

5.) Comments and opinions of One-hundred prominent physicians who used Krebiozen and found that the drug is safe and beneficial in the treatment of cancer. Among them are: DR. WALLACE GRAHAM, Major General and then Chief-of-Surgery in Walter Reed Hospital and Personal physician of President of the United States; DR. CHARLES BARRETT, Professor of Therapeutic Radiology Col. of Medicine Cincinnati and Director of the Tumor Clinic; DR. HUGH FULCHER, Professor of Neurosurgery, School of Medicine, Georgetown University and Chief Surgeon Grace Hospital Welsh, West Virginia; HENRY JAFFE, Professor of Pathology, New York Medical College; DR. VICTOR JOHNSON, Director of Mayo Graduate School of Medicine, Professor of Physiology, etc.; DR. CHARLES JOHNSON, Associate Professor of Clinical Pathology, Medical College of Virginia; DR. H. L. KAPLAN, Associate Professor of Internal Medicine, College of Medicine, Baylore; DR. LOUIS KRASNO, Assistant Professor Department of Medicine, Stanford; DR. WILLIAM M. LEES, Associate Professor Thoracic Surgery, Stritch School of Medicine, Loyola University; DR. H. C. LUETH, Clinical Professor College of Medicine, Illinois; DR. ALICE E. MOORE, Associate Professor of Biology, Sloan-Kettering Division, Cornell, Assistant and

Head of Sloan-Kettering Institute for Cancer Research; DR. LEON ARIES; DR. L. PAUL RALPH, Attending physician of the late Senator Arthur Vandenberg.

6.) Report of the Institute for Cancer Research and Lankenau Hospital Research Institute of Philadelphia (Ex. 23 to Plaintiffs' Reply Affidavit, submitted March 30, 1971), a leading cancer research institute whose reputation is known not only in the United States, but throughout the world. Experiments and observations were conducted by two prominent scientists, DR. STANLEY REIMANN and DR. THOMAS POMEROY on 40 patients, and they concluded:

> "Our conclusions on the material to date, though quite preliminary, are that it (Krebiozen) is non-toxic per se and has definite biologic activity specifically against tumor cells either directly or indirectly, or sufficient degree to warrant continued investigation of its mode of action with the hope that improvements may be made or some further knowledge concerning the biologic factors, controlling tumor growth may be contributed. Since this represents the first and only non-toxic chemical agent to show definite biologic activity of any degree against tumors of many types, it seems justifiable to encourage as much basic and clinical investigation as possible . . ."

Over this evidence, the Seventh Circuit Court chose to superimpose two affidavits, one of Dr. Jesse Steinfeld, Surgeon General and other of Dr. Carl Baker, Director of National Cancer Institute neither of whom ever used Krebiozen (Statement of Jesse Steinfeld in the Krebiozen trial, transcript page 9575, Ex. 21).

Dr. Steinfeld is an internist ("I was Board Certified in Internal Medicine in 1958"—Government Ex. 12.). Dr. Baker is a general practitioner ("I was licensed to practice

Medicine in the State of California"—Government Ex. 12). Neither Dr. Steinfeld nor Dr. Baker are cancer experts, because there is no board of experts in the field of cancer.

Their statements are negative statements and as such should not prevail over positive and credible testimony.

The Seventh Circuit opinion may now be *res judicata* in any future action which petitioners may wish to bring in the state courts of Illinois, with respect to the interpretation of "new drug" under the Illinois Act.

The issue, therefore, is one of life and death to those who are obtaining Krebiozen from physicians in Illinois and leads counsel to believe that it provides a sufficient basis for this Court to reconsider its denial of the petition for a Writ of Certiorari.

CONCLUSION

For the foregoing reasons, it is respectfully requested that this petition for rehearing be granted, and that upon further consideration, Writ of Certiorari issue to the United States Court of Appeals for the Seventh Circuit.

Respectfully submitted,

/s/ Solomon H. Friend
Solomon H. Friend
Attorney for Petitioners

Dated: New York, New York.

November, 1973.

CERTIFICATE OF COUNSEL

I, Solomon H. Friend, counsel for the above-named petitioner, do hereby certify that the foregoing petition for rehearing is presented in good faith and not for delay, and that it is restricted to the grounds specified in Rule 58 Subdivision 2 of the Rules of this Court.

/s/ *Solomon H. Friend*
Solomon H. Friend
Counsel for Petitioners

Of Counsel:

Anna R. Lavin
Edward J. Calihan, Jr.
Attorneys for Petitioners

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APPENDIX

ILLINOIS
Regular Session
Public Act 78-599, Laws 1973
Senate Bill No. 556
Received Oct. 23, 1973

AN ACT to amend Section 17 of the "Illinois Food, Drug and Cosmetic Act", approved June 29, 1967, as amended.

Be it enacted by the People of the State of Illinois, represented in the General Assembly:

Section 1. Section 17 of the "Illinois Food, Drug and Cosmetic Act", approved June 29, 1967, as amended, is amended to read as follows:

Section 17. (a) No person shall sell, deliver, offer for sale, hold for sale or give away any new drug unless (1) an application with respect thereto has been approved and the approval has not been withdrawn under Section 505 of the Federal Act, and (2) a copy of the letter of approval or approvability issued by the Federal Food and Drug Administration is on file with the Director, if the product is manufactured in the State of Illinois.

(b) No person shall use in human beings or animals a new drug limited to investigational use unless the person has (1) filed with the Federal Food and Drug Administration a completed and signed application "Notice of claimed investigational exemption for a new drug" in accordance with Section 130.3, and 130.3a of Title 21 of the Code of

Federal Regulations and the exemption has not been terminated and (2) filed with the Director, if any portion of the human or animal investigation is conducted in the State of Illinois, a form including but not limited to the following information: (a) name of person conducting the investigation; (b) type of drugs or chemicals used; (c) subjects (human or animal) of investigation; (d) location of investigation; and (e) purpose and expected results of investigation; such form shall be prescribed and furnished by the Department; and (3) the drug shall be plainly labeled in compliance with Section 505 (i) or 507 (d) of the Federal Act.

(c) This Section shall not apply:

(1) to any drug which is not a new drug as defined in the Federal Act; or

(2) to any drug which is licensed under the Public Health Service Act of July 1, 1944 or under the animal virus-serum-toxin law of March 4, 1913; or

(3) to any drug which is subject to Section 15 (1) of this Act.

Approved, September 7, 1973

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